ARCHIVES OF SURGERY

VOLUME 53 OCTOBER 1946 NUMBER 4

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TESTS FOR COLLATERAL CIRCULATION IN THE EXTREMITIES

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PRIOR to the introduction of the reactive hyperemia test by Matas,[1] there was no method of assaying before operation whether surgical occlusion of the great arteries would be followed by relatively adequate circulation in the extremity or whether some ischemic disaster would result. Indeed such precautions are still sometimes omitted, if one is to judge by the lack of mention of any tests for adequacy of collateral circulation in a number of reports and monographs dealing with the surgery of aneurysms and arteriovenous fistulas. It is our conviction that in general the age of the patient, the duration of the aneurysm or fistula and the general appearance of the affected extremity offer nothing conclusive in regard to the safety with which ligation of the involved vessel may be carried out. It is obvious that the ideal method of treating such lesions is to restore the continuity of blood flow by some type of reparative procedure rather than by ligation of the artery. Unfortunately, in spite of the advances in the restoration of damaged arteries by suture, end to end anastomosis and vein grafts, such procedures cannot be employed in many cases and when employed, cannot be counted on to function properly and permanently in every instance. Nothing is more important, therefore, than to attempt to evaluate beforehand the efficiency of the collateral circulation.

It is the purpose of this communication to review briefly some of the tests which have been used for estimation of the adequacy of collateral circulation and to point out the value and the shortcomings of such tests. We shall discuss in more detail the tests which we have found to be practicable and helpful. We have little new to present. In a large clinical study, however, certain merits and limita-

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1. Matas, R.: (*a*) Some of the Problems Related to the Surgery of the Vascular System: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries, Tr. Am. S. A. **28**:4-54, 1910; (*b*) Ann. Surg. **53**:1-43, 1911.

tions in the various tests for collateral circulation have come to light. It is hoped that these may prove useful to others. Our personal experience is based on tests of collateral circulation in approximately 275 patients with arterial aneurysms or arteriovenous fistulas whom we have treated by operation. We shall deal primarily with collateral circulation in the limbs, reserving the problem of testing collateral circulation to the brain for discussion in a subsequent publication.

Tests for adequacy of collateral circulation may be divided into those which can be carried out prior to surgical exploration and those which may be utilized at the time of operation. The former are of particular importance since on them depends the rational selection of the time for operation.

TESTS FOR COLLATERAL CIRCULATION WHICH CAN BE CARRIED OUT BEFORE OPERATION

The first practical method of estimating the efficiency of the collateral circulation was proposed by Matas in 1910.[1] Moskowicz [2] had introduced the reactive hyperemia test as a method for determining the safe level for amputation in cases of gangrene of the extremities. This consisted essentially in completely occluding the arterial circulation in the limb by tourniquet and in observing how far distally an adequate flush prevailed after release of such occlusion. Matas convinced himself that this procedure was not a test of the level of patency of the main arterial channels, as Moskowicz had supposed it to be, but rather of adequate capillary circulation. He adapted this method as a means of estimating the efficiency of collateral circulation in cases of aneurysm. It was carried out in this fashion: The aneurysm was stilled by application of a mechanical compressor applied over the artery proximally as near the lesion as possible. Having demonstrated the manner of obliterating pulsation in the aneurysm, the compressor was temporarily released, an Esmarch bandage was applied from the distal end of the extremity to the upper pole of the aneurysm and the compressor was reapplied. The Esmarch bandage was removed after five minutes, and the compressor was left in place. The progress, extent and intensity of the flush was observed. Matas specified no limit of time for development of an adequate flush but felt that the collateral circulation might be deemed adequate if a pink color returned to the hand or foot in a reasonable time. If color did not return in an hour, for example, he felt that one should undertake obliteration of the aneurysm with extreme caution. Gradually, through the years, the standards of this test have been made more rigid. Generally an adequate flush within three minutes is considered necessary if the

2. Moskowicz, L.: Die Diagnose des Arterienverschlusses bei Gangraena pedis. Mitt. a. d. Grenzgeb. d. Med. u. Chir. **17**:216-228, 1907.

collateral circulation is to be judged adequate.[3] We shall subsequently describe the test as we have carried it out and the standards which we have adopted.

Prior to the introduction of the reactive hyperemia test Korotkow[4] had suggested a test based on ionometric and sphygmomanometric movements of blood pressure in the digits during compression of the aneurysm. It was based on changes in color while the digits proximally were occluded with a manometer cuff. Matas found it unsatisfactory and abandoned it. We have had no experience with this procedure.

A test suggested by Quénu and Muret[5] is obviously hazardous and is mentioned only to be condemned. It consisted in cutting into the dorsal pedal artery during compression of the aneurysm to see whether bleeding would occur.

Among the three signs indicative of adequate collateral circulation suggested by von Frisch[6] was one which might serve as a preoperative test, namely, the persistence of normal color in hand or foot during compression of the aneurysm. This undoubtedly serves as a good index of adequacy of collateral circulation. Matas[1] had also utilized such observations. The chief difficulty with its execution is the maintenance of precise and complete compression of the aneurysm over a prolonged period. Often it is impossible to keep such exact occlusion of the desired portion of the artery for a long while with mechanical compressors, and with digital compression one's finger soon becomes exhausted.

The test of Tuffier and Hallion[7] consists in observation of venous filling in the hand or foot after the veins have been emptied by elevation of the part and then lowering of it to a horizontal level, with the aneurysm occluded by compression. As generally carried out, the limb is elevated 30 degrees until the veins are well emptied. The aneurysm is occluded by digital pressure, and the limb is lowered to a horizontal position after a blood pressure cuff at 60 mm. of mercury has been placed about the limb distal to the aneurysm. If the veins of the hand or foot fill within sixty seconds, collateral circulation is deemed

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3. Burns, Shock, Wound Healing and Vascular Injuries, Military Surgical Manuals, National Research Council, Division of the Medical Sciences, Philadelphia, W. B. Saunders Company, 1943.

4. Korotkow, cited by Matas.[1a]

5. Quénu and Muret: Sur le traitement moderne des anévrismes poplités, Rev. de chir., Paris **41**:282-294, 1910.

6. von Frisch, O.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefässverletzungen, Zentralbl. f. Chir. **41**:89-91, 1914.

7. Tuffier and Hallion: Sur un procédé permettent de prévoir que l'irrigation sanguine persistera dans un membre après ligature de son artère principale, Compt. rend. Soc. de biol. **73**:606, 1912.

adequate.[8] In discussing this test in his excellent review, Matas [8] stated that he found it difficult to employ because it was often rendered inaccurate by edema or venous stasis. We have found it of little practical help. Often the veins are so poorly filled, particularly in persons with pronounced vasospasm, that accurate estimation of venous filling time is impossible. In others, especially in patients with large arteriovenous fistulas, venous filling may occur promptly with compression of the fistula even while the limb is still elevated. And in others, venous stasis or edema interferes with the procedure.

Some have utilized the intradermal histamine test in order to estimate the efficiency of collateral circulation in cases of aneurysm. It is generally performed in this manner: The aneurysm is occluded by digital compression, and a drop of 1:1,000 solution of histamine phosphate is placed on the skin in the hand or foot. The skin is needled through the drop so that a wheal develops. This should appear in from three to five minutes. The prompt occurrence of a flare prior to development of the wheal is probably fully as important as the development of a wheal. Having found the histamine test not particularly helpful in the determination of the safe level of amputation in cases of gangrene, we have not utilized this test for study of collateral circulation in cases of aneurysm. The intradermal salt solution test is, in our opinion, impractical, since the wheal should persist for nearly an hour if the circulation is good and since accurate compression of the artery for such a length of time is most difficult.

If the aneurysm has brought about cessation of pulsation in the arteries distal to the lesion and if the extremity is well nourished, it may be fairly safely assumed that the collateral circulation is adequate. This observation is known as Delbet's sign.[9] We have found it to be useful in a number of instances. It is often present in huge subcutaneously ruptured aneurysms in which other tests for collateral circulation cannot be carried out satisfactorily because of the huge size of the aneurysm and because tenderness and pain on pressure often preclude compression of the artery. One case which may serve to question the complete reliability of the sign will be discussed subsequently.

A number of other means of estimating the efficiency of collateral circulation come to mind. We have checked the time in seconds necessary for the return of color to an area of a finger or toe blanched

8. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries: Further Observations, with Special Reference to the Author's Methods, Including a Review of Other Tests Thus Far Suggested, J. A. M. A. **63**:1441-1447 (Oct. 24) 1914.

9. Delbet, P.: Extirpation d'un anévrisme poplité: Guérison, Bull. et mém. Soc. de chir. de Paris **35**:865-870, 1909.

by digital pressure and compared it with the time required for return of color without compression of the aneurysm and with the results of the same test in the normal contralateral limb. Similarly, we have milked the blood from the subpapillary venous plexus by rolling a snug rubber band from the tip of a digit to its base and checked the time for return of color after release of the constricting band during compression of the aneurysm.[10] Though the results from such tests as these often fit in with the deductions arrived at from the reactive hyperemia and other tests, we have not found them sufficiently helpful to continue their usage routinely. One might utilize the fluorescein test of Lange and Boyd[11] during compression of the artery. Our limited experience with fluorescein in determination of the adequacy of circulation in pedicle grafts and similar conditions has not been sufficiently encouraging to lead us to apply the method in cases of aneurysm. Should further studies prove its general reliability, it may be advisable to carry out such experiments in cases of aneurysm.

TESTS APPLICABLE AT THE TIME OF OPERATION

The test most widely known and utilized is the observation of pulsation in or free flow of blood from the distal end of the involved artery during occlusion of the proximal artery. This is known as the Coenen-Henle phenomenon.[12] Good retrograde pulsation in the distal artery is a comforting sign and is certainly indicative of good collateral circulation. The observation of free flow of blood can, of course, be made only after the aneurysm is opened, which is inadvisable unless one already has reasonable assurance that collateral circulation is satisfactory. Furthermore, as we shall develop subsequently, it is not a reliable indication of adequacy of collateral circulation.

Von Frisch[6] suggested that venous stasis below the clamped vein with the involved artery occluded was indicative of good collateral circulation. This cannot be relied on, as the tension of the vein varies not only with the efficiency of the collateral circulation but also with the state of venous filling at the time the vein is obstructed and with the adequacy of collateral venous circulation about the obstructed segment of vein.

In our experience, the most trustworthy information obtainable at the time of operation is observation of the color and warmth of the

10. Suggested by Major David I. Abramson.

11. Lange, K., and Boyd, L. J.: The Use of Fluorescein to Determine the Adequacy of the Circulation, M. Clin. North America **26**:934-952, 1942.

12. Coenen, H.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefässverletzungen, Zentralbl. f. Chir. **40**:1914-1916, 1913. Henle, A.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefässverletzungen, ibid. **41**:91, 1914.

hand or foot during a prolonged period of occlusion of the involved artery. If the hand or foot maintains fairly normal color and warmth during a period of twenty to thirty minutes of temporary occlusion of the artery at the site where ligation will be necessary in order to effect a cure, one can be reasonably certain that the collateral circulation is adequate.

PERSONAL EXPERIENCES WITH TESTING THE COLLATERAL CIRCULATION

As mentioned in the preceding discussion, we have come to feel that the reactive hyperemia test is the most practical and reliable test which can be carried out before operation. We have employed it in the following manner: The limb is elevated. The hand is blanched thoroughly by having the patient make a tight fist. The foot is blanched by milking of the blood from the foot by the application of pressure with both hands on the dorsal and plantar surfaces and the moving of this palmar compression back toward the heel and up to the ankle. This procedure is repeated if necessary until good blanching is obtained. A similar procedure is used for hands in which motor paralysis prevents the making of a tight fist. When adequate blanching is obtained, a blood pressure cuff, previously applied about the limb distal to the aneurysm or fistula, is quickly inflated to a pressure of from 200 to 220 mm. of mercury. This provides complete interruption of arterial inflow below the level of the cuff. The hand or foot becomes extremely pale. The limb is lowered to a comfortable horizontal position. The observer has previously determined the most distal point at which digital compression of the artery completely stills the aneurysm or fistula. This is checked by palpation and auscultation, and one makes certain that such compression obliterates completely the pulsation, bruit and thrill in the aneurysm. In order to facilitate accurate observation of changes in color in the hand, foot or distal end of the extremity and at the same time of the successful obliteration of blood flow through the aneurysm or fistula, the test is always carried out by two observers. Four minutes after application of occlusive pressure in the blood pressure cuff the aneurysm or fistula is again compressed, and pressure is maintained during the remainder of the test. During this time, absence of bruit, thrill and pulsation is checked constantly by auscultation and palpation. Five minutes after the cuff has been inflated it is suddenly released, and the rapidity, completeness and intensity of the resulting flush are determined. The flush reaches the most distal portions of the extremity, the digits, if they are present, last. The number of seconds which elapse before hyperemia begins in these parts is recorded. We also

record the number of seconds which elapse before the flush becomes complete in extent and intensity. Digital compression of the artery is maintained for only two minutes after release of the blood pressure cuff. It is then noted whether there is any further improvement in the completeness or intenseness of the hyperemia. If a full and complete hyperemia occurs in less than two minutes, the collateral circulation is felt to be adequate.

Matas determined that the test could be carried out with a blood pressure cuff rather than an Esmarch bandage but felt that the latter was preferable, because he thought that its use brought about a more complete deprivation of blood and consequently a more intense reactive hyperemia. We have adopted the aforementioned method of blanching the limb and of obstructing blood flow for several reasons. In the first place, it is carried out more simply and quickly than with the use of an Esmarch bandage. In the second place, if we place the cuff somewhat distal to the aneurysm rather than bring an Esmarch bandage up to its proximal pole, we feel that it is possible by auscultation and palpation to be more certain that the aneurysm is stilled or the fistula obstructed. Compression by an Esmarch bandage is reserved for the rare instances in which adequate blanching of the limb cannot be otherwise achieved—and then it is only used to milk the blood out of the limb—while obstruction of blood flow is maintained by the inflated blood pressure cuff. We compress the artery digitally rather than by means of a mechanical compressor, since we feel that the artery can thus be more accurately occluded and with less hazard of compressing adjacent collateral vessels at the same time. The custom of having the test performed by two persons in order to permit constant and careful observation of the completeness of obliteration of the aneurysm or fistula by auscultation and palpation cannot be emphasized too strongly. Should compression be incomplete and some blood flow proceed through the compressed vessels, faulty deductions as to the efficacy of the collateral circulation might be made, with disastrous consequence.

The site of compression deserves consideration. The most distal point at which compression of the artery brings about cessation of pulsation, bruit and thrill represents that portion of the artery which opens into the aneurysmal sac or communicates with the vein or sac in instances of arteriovenous fistulas. It is at this point that the artery will have to be ligated at operation unless some reparative procedure can be carried out. Compression at some point proximal to this, though it may bring about cessation of pulsation, bruit and thrill, may give misleading information. We have attempted to illustrate this diagrammatically in figure 1. Proximal compression may occlude

blood flow through collateral vessels, which may be preserved in case operative ligation is necessary (fig. 1*A*). In such a case the test would demonstrate less adequate collateral circulation than actually exists. On the other hand, compression of the artery proximal to the aneurysm may leave open collateral channels which may necessarily have to be sacrificed at operation (fig. 1 *B*). In such an instance the test would lead one to believe that the collateral circulation was better than was actually the case.

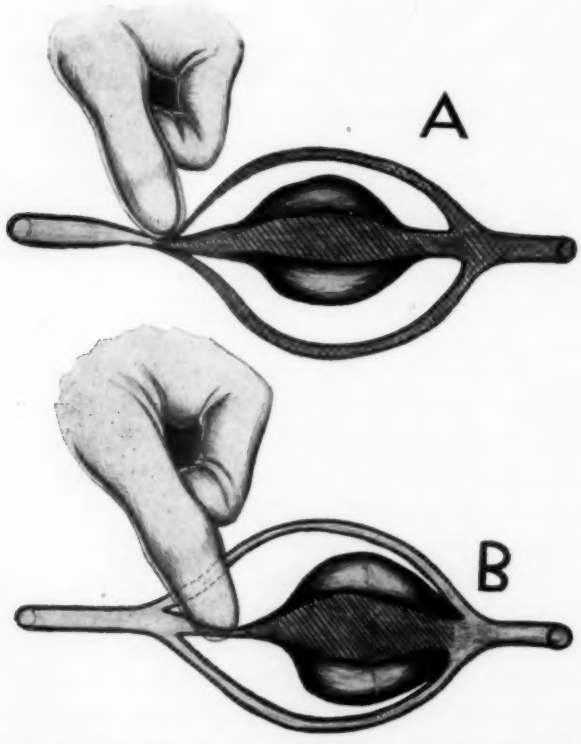

Fig. 1.—Diagrammatic representation of errors which may result from occlusion of the artery proximal to the aneurysm. In *A* an effort is made to demonstrate the possibility of occlusion of collateral channels which may be spared at operation. This would lead one to judge the collateral circulation to be less adequate than it actually was. *B* represents an effort to demonstrate the possibility of leaving open during the test collateral channels which actually arise from the aneurysm itself and must be sacrificed in extirpation of the aneurysm. If these vessels are small they may remain open, and yet at the same time pulsation and bruit may be absent. Such an occurrence might lead one to feel from the test that the collateral circulation was better than was actually the case.

One problem of considerable importance concerns the basal conditions under which the test is carried out. Reactive hyperemia is better when the limb tested is in a state of vasodilatation rather than of vasoconstriction. In the absence of sympathetic denervation, limbs in

which aneurysms or arteriovenous fistulas occur are capable of a wide variation in vascular tonus, just as are normal limbs. Should the test be carried out under ordinary conditions and at the ordinary temperature of the ward or under conditions conducive to vasoconstriction or vasodilatation? We have repeatedly demonstrated significant difference in the results of the reactive hyperemia test under ordinary conditions in a ward, during extreme vasoconstriction and during full vasodilatation, by repeating the test on a given patient under these varying conditions on the same day. In general, the test shows evidence of poorer collateral circulation during vasoconstriction and of better collateral circulation during vasodilatation. Since the patient is destined to live in the environment of a ward after operation and since constant maintenance of full vasodilatation cannot be assured unless sympathectomy is performed, it is our feeling that the procedure is best carried out without effort to induce either vasoconstriction or vasodilatation.

There are certain errors which occasionally enter into the test and result in inaccurate estimation of the efficiency of the collateral circulation. These errors prevail in all tests which depend on compression of the involved segment of artery. In the first place, this may result from improper localization of the lesion or, to express it in another manner, from simultaneous compression of an uninvolved main arterial stem during compression of the affected minor artery. For example, in a 24 year old patient with a five month old arteriovenous fistula in the popliteal fossa, pressure sufficient to obliterate the bruit and thrill invariably resulted in loss of pulsation in the dorsal pedal and posterior tibial artery and study of collateral circulation gave results suggesting entirely inadequate collateral circulation. Repetition of these tests showed no improvement with the passage of time and with intermittent occlusion of the fistula by compression. Five weeks after admission a lumbar sympathectomy was performed, after which the flush during the reactive hyperemia test was prompter and of greater intensity. Six weeks after operation the collateral circulation was judged to be adequate and operation was done. On exploration, the fistula was found between the inferior geniculate artery and the overlying popliteal vein rather than between the popliteal artery and vein, as had been suspected beforehand. The fistula was so close to the popliteal artery that it could not be occluded by digital compression without occlusion also of the popliteal artery. The fistula was easily excised without disturbing the popliteal artery. We have attempted to illustrate our experience with tests for collateral circulation on this patient in figure 2.

Similarly, another 24 year old patient, with signs of an arteriovenous aneurysm of four months' duration in the sternoclavicular region, lost

his brachial and radial pulse during each compression of the fistula. Again collateral circulation was judged inadequate according to all studies. After four weeks of further observation and intermittent compression, he was subjected to dorsal sympathectomy, following which the reactive hyperemia test indicated good collateral circulation. At operation the fistula was found between the transverse cervical artery and the proximal end of the internal jugular vein instead of between the subclavian vessels, as we had anticipated. The fistula could be excised without interference with the subclavian vessels. Had

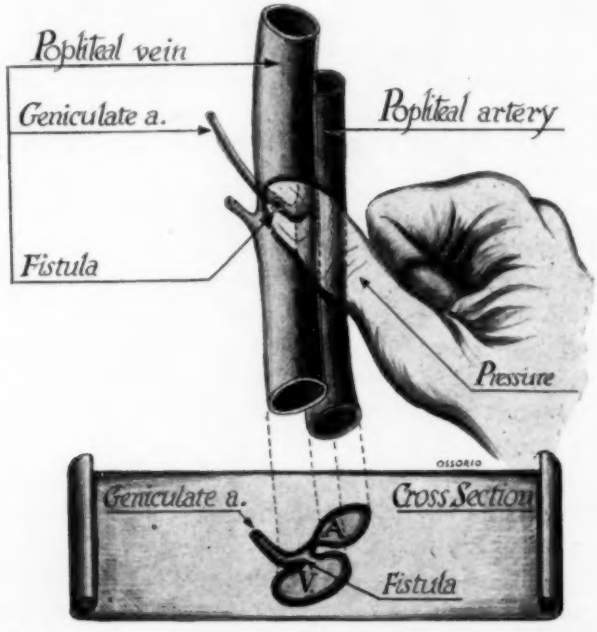

Fig. 2.—Semidiagrammatic drawing of the findings in a patient with a fistula between geniculate artery and popliteal vein. It was impossible to compress the fistula without at the same time occluding the adjacent popliteal artery.

it been possible to compress the fistula itself in these 2 cases without also compressing a more important adjacent artery, both of the patients might have had correct localization before operation and might have been spared sympathectomies. Lesions in the proximal portion of the profunda femoral vessels constitute one of the most difficult problems in correct localization of fistula or aneurysm and in correct testing of the collateral circulation. In order to obliterate the fistula or still the aneurysm by direct pressure, almost invariably the overlying superficial femoral artery must be compressed, with resultant error in localization and in interpretation of the efficacy of collateral circulation.

Conversely, if one can definitely establish the fact that the lesion is in a minor vessel and can demonstrate that pulsation, bruit and thrill can be eliminated by pressure, with preservation of blood flow in the main arterial stems, one has little worry concerning the nutrition of the part following excision. Often careful repeated examinations will enable one to make correctly such a localization even when the lesion is near the main artery. For example, in patients who presumably have axillary arteriovenous fistulas or aneurysms, it is often possible to demonstrate that the lesion actually involves the thoracoacromial trunk, the subscapular vessels or other branches. A word of warning, however, is necessary in this regard. In a single instance, the lesion involved not only a minor branch but also the main artery. The patient was a 41 year old soldier who had an arteriovenous fistula, of six months' duration, which was thought to involve one of the circumflex humeral vessels. The bruit and thrill could be eliminated by direct pressure without disturbing the brachial pulse. At operation it was found not only that the anterior circumflex humeral artery and vein communicated through a small sac but that the superior portion of the axillary artery opened into this sac through a large fistula. It had been possible to compress the sac in such a manner that the openings from the two arteries and the vein were occluded without compression of the axillary artery itself. Ligation was necessary because the damage to the axillary artery was too extensive to permit repair. Consequently, the efficacy of the collateral circulation had to be established during the operation by observation of the color and warmth of the hand during prolonged temporary occlusion of the axillary artery with a rubber-shod clamp.

Another manner in which the tests may indicate a poorer collateral circulation than actually exists is through the inadvertent compression of collateral channels which are actually uninvolved and can be spared during operative excision of the lesion. In our experience this has apparently occurred chiefly from transmission of pressure through the laminated thrombus in a saccular aneurysm. We have attempted to illustrate this in figure 3. It is exemplified by the following case: A 20 year old patient with a traumatic popliteal arterial aneurysm of three months' duration had inadequate flush during the reactive hyperemia test. He had no significant improvement in this test during the next five and one-half weeks. Lumbar sympathectomy was performed, following which the test indicated somewhat better but still inadequate collateral circulation. After repeated observations the aneurysm was explored, approximately eight months after the initial injury. It was explained beforehand to the patient that if during temporary occlusion of the artery at the site of the aneurysm the foot should show ischemic

changes nothing more than a partial proximal ligation could be done. At operation it was found that the artery could be occluded over a prolonged period, with maintenance of good color and warmth in the foot. The aneurysm was large and contained an extensive laminated thrombus. It was apparent from its character and position that pressure on the artery sufficient to still the aneurysm had occluded the geniculate branches by transmission of pressure through the wall of the aneurysm. The aneurysm was excised, with ligation of the involved artery and with preservation of the geniculate branches. The patient maintained a warm, well colored foot.

The same error in interpretation of the collateral circulation may result from the presence of collateral channels in such a position that the aneurysm cannot be stilled by pressure without also directly compressing the collateral vessels. Our experience with a 23 year old soldier who had a traumatic axillary arterial aneurysm of three months'

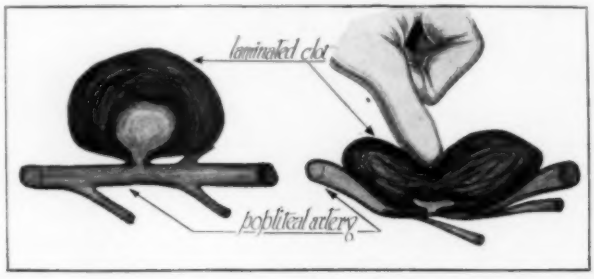

Fig. 3.—In this drawing we have attempted to illustrate the occlusion of uninvolved collateral channels by transmission of pressure through the laminated thrombus within the sac. In such cases preoperative tests indicate poorer collateral circulation than actually exists.

duration illustrates this mechanism. He had a large aneurysm in the third portion of the axillary artery and pronounced impairment of function of the brachial plexus. His collateral circulation was inadequate as judged by the reactive hyperemia test. Because of the damage to the nerves, it was felt advisable to do everything possible to render the collateral circulation adequate so that operation could be carried out as soon as possible. Three weeks after admission a dorsal sympathectomy was performed, and intermittent digital compression was given from time to time. The reactive hyperemia test continued to reveal evidence of insufficiency of collateral circulation. With the patient's understanding that nothing more than partial proximal ligation might be feasible, the aneurysm was explored approximately two months after sympathectomy. With direct visualization it was understandable why the test for collateral circulation had indicated insufficient collateral circulation. The aneurysm was large. The radial, ulnar, and median

nerves were stretched over the surface of the sac and were compressed by it. There was a large collateral artery which emerged proximally from the axillary artery and passed directly over the aneurysmal sac only a few millimeters away from the involved portion of the axillary artery. It was apparent that compression sufficient to still the aneurysm would have also necessarily interrupted blood flow through this large collateral channel. The hand remained warm and of excellent color during prolonged temporary occlusion of the axillary artery with a rubber-shod clamp. The aneurysm was excised, and appropriate operation for the injuries to the peripheral nerve of the patient was carried out. The collateral vessel mentioned was saved. It was possible to excise the damaged portion of the axillary artery and reconstruct it by means of end to end suture.

Thus far we have discussed errors in testing which might lead to the impression that the collateral circulation is poorer than it actually is. Such errors are troublesome. They cause an unnecessary delay in operative cure of the aneurysm and untold worry to the surgeon. Nevertheless, if properly handled, they will not jeopardize the involved limb. The contrary is obviously true in case an error in testing efficiency of collateral circulation leads to the false assumption that it is adequate. A single instance of this sort has occurred in our experience, the only case in which operative excision of an aneurysm has been immediately followed by obviously insufficient circulation with steady death of tissue and ultimate gangrene of the distal third of the foot. The patient was a 35 year old soldier who had a popliteal arteriovenus fistula of two and one-half months' duration. There was practically no flush of the foot during the reactive hyperemia test performed under ordinary conditions, but there was a great deal better flush during reflex vasodilatation. Three weeks after admission a lumbar sympathectomy was carried out, following which there was a good flush during the test. The popliteal vessels were explored about four months after the patient had sustained his injury. Immediately prior to operation he had shown a good hyperemia which began in his toes in twenty seconds and became complete in exactly two minutes. The condition found at operation is illustrated in figure 4. Not only was there a direct communication between the popliteal artery and vein, but there was a saccular arterial aneurysm as well and a large geniculate artery emerged from the aneurysmal sac proximal to the fistula. It seemed entirely likely that digital compression had occluded the fistula and had not occluded blood flow through this geniculate artery. In order to remove the aneurysm it was necessary, however, to sacrifice this vessel. This was done, the involved segment of the artery and vein being excised. The postoperative course has

been described. It was felt that in all likelihood misleading information had been obtained from the reactive hyperemia test.

Since the patient had shown what we thought to be a good and complete flush just two minutes after release of the constricting blood pressure cuff during the reactive hyperemia test and had suffered such an ischemic disaster following excision, we felt it necessary to revise our standards of this test. Up to this time, we had considered an intense

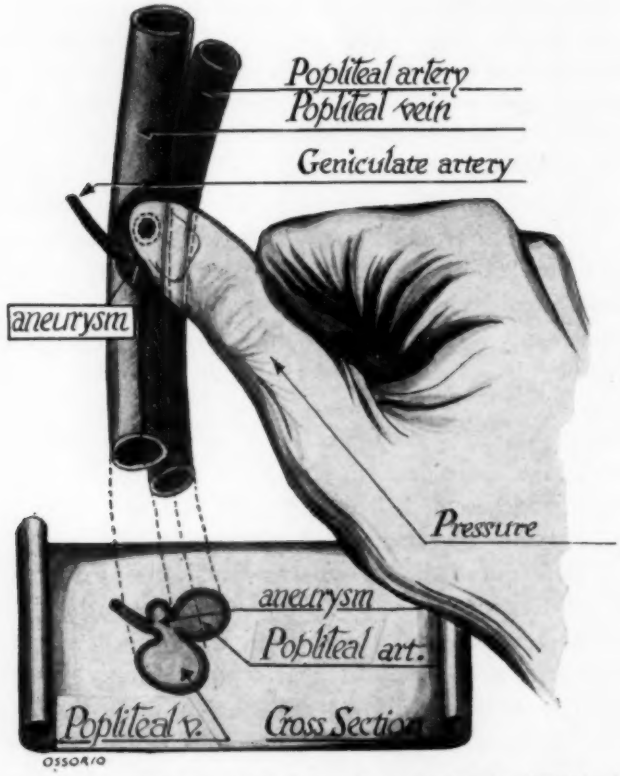

Fig. 4.—In this drawing an effort is made to depict the findings in a patient in whom the collateral circulation was judged better than it actually was. In all likelihood, digital compression occluded the fistula successfully but left open a large geniculate branch which emerged from the aneurysmal sac and had to be sacrificed in extirpation of the aneurysm.

and complete flush within three minutes as evidence of satisfactory collateral circulation. Since then, we have felt that a full, complete flush must prevail in less than two minutes, with no further significant improvement on release of pressure from the artery, before the collateral circulation is considered to be adequate.

This patient illustrated another most important point. Since we had felt that the collateral circulation was adequate from the preoperative

tests, his feet were not draped so that they could be observed during the operation. Had this precaution been taken and the color and the warmth of the feet been observed during temporary occlusion of the involved vessels below and above the site of the fistula, we should undoubtedly have noticed changes in color and perhaps temperature which would have made it apparent that excision of the lesion should be deferred. Since that time it has been our policy to expose the hand or foot in every instance in which there is the slightest question as to the adequacy of collateral circulation and to make certain that the color and warmth of the part remain good during prolonged occlusion of the involved artery with a rubber-shod clamp. This experience further illustrates the previously mentioned fact that the free flow of blood from the distal artery is not necessarily a definite sign that collateral circulation is adequate, for at operation the patient had fairly good retrograde bleeding from, although no pulsation in, the distal end of the artery.

It is important to inquire whether any evidence which testifies to the validity of the reactive hyperemia test has been accumulated. This is a most important question and one which is exceedingly difficult to answer on the basis of clinical experience. Certain observations, however, suggest that the test is generally reliable though not infallible. In the first place, with one exception previously mentioned and with a second possible exception to be discussed subsequently, all the patients who have had tests suggesting adequate collateral circulation have maintained excellent circulation following operative obliteration of the aneurysm or fistula. In the majority of these patients, the involved artery was ligated. They have maintained good warmth and color of the extremity and have not had, even for a brief period, any sensory or motor loss or other evidence of ischemia. In the 1 instance of gangrene, previously described, the findings at operation suggested a possible adequate explanation for the misleading information derived from the preoperative test.

In the second place, some confirmation of the validity of this test is obtained from experience with the patients who had evidence of inadequate collateral circulation at the time that the aneurysm was cautiously explored. In all but 1 of these patients, study of the circulation in the hand or foot during a prolonged period of temporary occlusion of the artery revealed evidence of adequate collateral circulation. In the great majority there prevailed some anatomic situation which offered a reasonable explanation of the misleading preoperative reactive hyperemia tests. Certain of the anatomic mechanisms involved have been discussed.

In the third place, some more precise information concerning the accuracy of the test is derived from our experience with 2 patients.

The first was a 37 year old man who had a traumatic arterial aneurysm of the proximal portion of the popliteal artery. Reactive hyperemia study showed practically no flush. Up to this point our experience with increasing the efficacy of collateral circulation by means of sympathectomy had been so uniformly successful that at the time we held too optimistic a view concerning its value. The aneurysm was consequently explored, and its cure necessitated ligation of the artery. The foot was cold and blue following this procedure and was much the same following a sympathectomy which was performed immediately after excision of the aneurysm. The foot remained rather cold for several hours, and then the color and warmth returned to normal. However, during this interval of ischemia, ischemic nerve paralysis had developed, which weakened all the movements of his foot and paralyzed extension and which resulted in hypesthesia or anesthesia of the distal third of the leg and foot. Fortunately he recovered satisfactorily from this disability. This ischemic difficulty following operation in the face of poor reactive hyperemia tends to confirm the reliability of this test. The second patient was a 27 year old man with a femoral arteriovenous fistula. Three and one-half months after injury a lumbar sympathectomy was performed, because the reactive hyperemia test showed practically no flush. This study, frequently repeated after sympathectomy, continued to indicate poor collateral circulation. This was not altered by frequent intermittent occlusion of the artery. The aneurysm was explored six months after injury, and at the time of operation the involved segment of the artery was occluded with a rubber-shod clamp. The foot immediately became pale and after some minutes was completely white. The wound was closed without excision of the aneurysm. This confirmation on the operating table of the poor collateral circulation also serves to establish the validity of the reactive hyperemia test.

These observations all tend to confirm the reliability of the reactive hyperemia test. It must be stated, however, that exploration has been carried out in a few instances in which nothing was found at operation to explain the discrepancy between a poor preoperative test and the actual presence of adequate collateral circulation. In these few cases preoperative study had indicated poor or questionable collateral circulation. During the precise temporary occlusion of the involved artery at operation, excellent color and warmth had been maintained in the hand or foot and excision of the lesion with ligation of the artery was followed by good circulation. These cases are few but are important, since they reveal the fact that the reactive hyperemia test as we have employed it is not infallible. We conclude that this procedure is practical and helpful, though sometimes misleading. It would be most desirable to

check the reliability of this test in experimentation on animals, in which accurate controls would permit more convincing deductions.

We have mentioned beforehand that numerous other tests for collateral circulation have been utilized which are not considered sufficiently helpful to warrant their routine use, though they often confirm the reactive hyperemia test. Two observations have, however, been found to be helpful. The first is the observation of the color and warmth of the hand or foot during prolonged compression of the involved artery. We have referred to the difficulties involved in carrying out this test properly. In the interpretation of the results of this study, it is important to assay the circulatory status of the hand or foot in positions other than the horizontal one. We have found pronounced pallor of the hand on elevation when the color and warmth remained excellent in the horizontal position during a period of thirty minutes of compression. The second is Delbet's sign. We have seen nothing to suggest that if the arterial pulses have been lost in an extremity distal to an aneurysm and the limb has maintained good circulation ligation of the artery entails any hazard of ischemic difficulty. We have studied 1 patient who had definite evidence of impaired circulation in a limb in which all pulses distal to a large subcutaneously ruptured femoral aneurysm were absent. The patient had lost tibial and saphenous sensation, though no motor function. He was in great pain. A sympathectomy was performed, following which the previously poor reactive hyperemia was excellent. Aneurysmorrhaphy, with ligation of the artery, was immediately performed. After operation, the foot maintained excellent color and warmth but some peroneal sensory loss was added to the existing sensory difficulty. Motor function remained intact. Because of the excellent color and warmth of the foot, it was hard to explain this added sensory difficulty on an ischemic basis. Conceivably, further damage to the already injured sciatic nerve may have resulted from the temporary use of a tourniquet. Difficult as this complication is to explain, it is cited as an example of postoperative sensory loss, possibly on an ischemic basis, in a limb having evidence of impaired circulation and no pulses distal to the aneurysm.

With regard to the tests applicable at the time of operation, we have previously commented on the probable reliability of good retrograde pulsation in the distal artery, the unreliability of retrograde bleeding without retrograde pulsation and the errors inherent in interpretation of venous stasis below the clamped vein during occlusion of the involved artery. In our experience the most reliable sign is the maintenance of relatively good color and warmth of the hand or foot during occlusion of the involved segment of artery with a rubber-shod clamp. This observation should, we feel, extend over a period of at least twenty,

and preferably thirty, minutes. It should be emphasized that if the operation is performed with the patient under spinal or general anesthesia this test indicates adequacy of collateral circulation during inhibition of vasoconstrictor impulses. Conceivably the collateral circulation might not be satisfactory if vasoconstriction should occur. If an aneurysm or fistula is treated and ligation of the artery is performed on the basis of such an observation, one should be prepared to eliminate sympathetic impulses should circulation be subsequently compromised by vasoconstriction.

Finally, it should be stated that all the tests which have been discussed are based on the assumption that the existing collateral channels will remain patent. Should they be occluded subsequently by thrombosis, disaster may occur. We have had the misfortune to have one example which illustrates this difficulty. A 25 year old patient with a femoral arteriovenous fistula had evidence of good collateral circulation. Eight and one-half months after injury the fistula was explored. While the involved segment of the artery was occluded with a rubber-shod clamp, the foot maintained good color. The fistula was excised, with ligation of the femoral artery just below the point where the profunda originates. The circulation in the foot was satisfactory until the sixth postoperative day, when pain suddenly developed in the popliteal space, calf and foot, and pronounced hypesthesia of the foot developed. Subsequently edema developed, and it was apparent on examination that the patient had undergone thrombosis of some of the arterial collateral vessels and extensive thrombosis of the deep veins of the calf. Within a few hours after this accident, a sympathectomy was performed. Despite the fact that it improved the circulation somewhat, gangrene of the toes and sole developed, necessitating amputation.

COMMENT

The determination of the adequacy of collateral circulation prior to exploration for aneurysm or arteriovenous fistula is most important. We feel that the most reliable and practical preoperative test for collateral circulation is the reactive hyperemia test. Though of great practical help and general reliability, this test is not infallible. The chief difficulties arise from the occasional impossibility of accurate compression of the involved arteries at the exact site of the fistula or aneurysm without concomitant compression of neighboring uninvolved vessels. If an excellent and complete flush occurs promptly during the test, with no further improvement on release of the compressed artery, one may approach the aneurysm and ligate, if necessary, the involved artery, with minimal risk of ischemic difficulty.

If the reactive hyperemia test indicates borderline or poor collateral circulation, every effort should be made to bring about improvement in the collateral circulation prior to exploration. If one does not succeed in establishing collateral circulation which is adequate according to this test, exploration should be carried out with great caution. The hand or foot should be exposed during operation and should be observed for change in color and temperature during prolonged temporary occlusion of the involved segment of artery. If ischemia of the hand or foot prevails, extirpation of the lesion should be deferred unless it is perfectly evident that a cure can be effected with maintenance of continuity of the involved artery.

Continued good circulation in the extremity during prolonged compression of the involved segment of artery is a somewhat difficult but useful confirmatory preoperative test. The absence of pulses distal to an aneurysm or fistula in a limb which maintains good circulation is indicative of adequacy of the collateral circulation.

All preoperative study of collateral circulation is based on the premise that no collateral vessels will be needlessly destroyed during operation and that no postoperative thrombosis will occur.

Though present methods of study render operation on aneurysms fairly safe, it is hoped that future investigation will produce more precise means of estimating collateral circulatory adequacy.

SUMMARY

Various methods for testing the efficiency of collateral circulation have been reviewed, and those which we have found most useful have been discussed in detail. An effort has been made to point out the utility of these procedures and at the same time to indicate their pitfalls and limitations.

Technician Fifth Class A. Ossario made the illustrations.

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EFFECT OF PENICILLIN IN EXPERIMENTAL INTESTINAL OBSTRUCTION

Cure of Strangulated Ileal Obstructions Treated with Penicillin Prior to Late Resection

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EXPERIMENTAL evidence for the importance of the role played by bacteria in producing "toxemia" and death in intestinal obstruction is briefly as follows: Dogs having isolated obstructed jejunal loops will die from a rather characteristic train of symptoms within a few days, usually four or five.[1] When penicillin is either placed in such loops or administered parenterally to dogs in which such loops have been constructed, these dogs will be protected from "toxemia" and death for a significant period, sometimes for over a month.[2] Succinylsulfathiazole, which is absorbed more slowly from isolated loops, will also protect animals with isolated obstructed loops when placed in the loops at the time of operation.[3] One such dog was allowed to survive for over a year.[3b] Prior to the advent of potent antibacterial drugs for experiments of this type, the importance of bacteria as the cause of death was strongly suspected on the basis of a process of exclusion by such investigators as Davis and Stone,[4] Murphy and Brooks [5]

From the Surgical Hunterian Laboratory of the Johns Hopkins University School of Medicine and the Johns Hopkins Hospital.

1. Stone, H. B.; Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, Bull. Johns Hopkins Hosp. **23**:159-165 (June) 1912.

2. Harper, W. H., and Blain, A., III: The Effect of Penicillin in Experimental Intestinal Obstruction: Preliminary Report on Closed Loop Studies, Bull. Johns Hopkins Hosp. **76**:221-244 (June) 1945.

3. (*a*) Poth, E. J., and Firor, W. M.: Unpublished data. (*b*) Harper, W. H., and Blain, A., III: Unpublished data.

4. Davis, D. M., and Stone, H. B.: Studies on the Toxicity in Intestinal Secretion, J. Exper. Med. **26**:687-691 (Nov.) 1917.

5. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, Arch. Int. Med. **15**:392-412 (March) 1915.

and, especially, Dragstedt.[6] In 1944, the efficacy of prophylactic succinylsulfathiazole in protecting dogs having ileal lesions produced by occlusion of mesenteric veins but in which the lumen of the bowel was not obstructed was reported.[7]

In a recent communication by Blain and Kennedy[8] experiments demonstrating the striking but limited protection afforded by massive doses of penicillin in dogs with strangulated obstructions of the lower part of the ileum were described.

This present report is concerned with an account of 5 dogs in which resection of a strangulated ileal obstruction was performed at a period twice as long after the production of the strangulation as any control dog, not treated with penicillin, lived. Four of these resections were completely successful, and the dogs were cured. Two of the dogs in which resections were performed, as well as their controls, were mentioned previously.[8]

EXPERIMENTAL METHODS

The details of the experimental procedures utilized in these studies were given in the previous report by Blain and Kennedy.[8] The fundamental steps were as follows: Strangulated obstruction in each of 5 control dogs and 5 treated dogs was produced in the following manner. With the animals under anesthesia induced by pentobarbital sodium given intravenously, a right rectus incision was made, and through this the terminal part of the ileum was delivered. At a point just proximal to the termination of the antimesenteric artery the bowel was transected between clamps, and each of the two ends was inverted by the closed method of Parker and Kerr. The mesenteric veins to a 60 cm. segment of the proximal part of the ileum were occluded with double silk ties, as were the arteries and veins running parallel to the bowel toward the selected segment. At either end of the segment to be strangulated, the mesentery was divided down to its base in order to preclude the development of any collateral venous channels.

All dogs were starved for twenty-four hours prior to operation, and food and fluids given orally were withheld postoperatively until after the second operation (resection and anastomosis), which was performed in the dogs treated with penicillin. Cultures of the lumen bowel were made in dogs to be treated with penicillin. At autopsy of all the dogs which died, cultures were taken of the obstructed bowel, the heart blood and the peritoneal transudate which developed as a result of the strangulation. In all cases the strangulated segment of ileum measured at least 50 cm. at the end of the operation, and in all cases this segment

6. Dragstedt, L. R.; Moorehead, J. J., and Burcky, F. W.: Intestinal Obstruction: An Experimental Study of the Intoxication in Closed Intestinal Loops, J. Exper. Med. **25**:421-439 (March) 1917.

7. Sarnoff, S. J., and Poth, E. J.: Intestinal Obstruction: I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion, Surgery **16**:927-931 (Dec.) 1944. Sarnoff, S. J., and Fine, J.: The Effect of Chemotherapy on the Ileum Subjected to Vascular Injury, Ann. Surg. **121**:74-82 (Jan.) 1945.

8. Blain, A., III, and Kennedy, J. D.: The Effect of Penicillin in Experimental Intestinal Obstruction: Studies on Strangulated Low Ileal Obstructions, Bull. Johns Hopkins Hosp. **79**:1-20 (July) 1946.

was cold and black or deep purple and had begun to exude sanguinous fluid when returned to the abdomen. At autopsy or at the operation for resection the affected segment was always found to be black or dark purple, heavy and edematous and distended and stretched, so that it measured at least 70 cm. in length, and its walls showed varying degrees of necrosis.

Immediately following the operation in which obstruction and strangulation were produced, each dog was given 500 cc. of whole blood intravenously and 500 cc. of isotonic solution of sodium chloride subcutaneously. Prior to operation blood was taken for a determination of the hematocrit level. This was repeated at intervals after operation, and a fall of 5 degrees in the hematocrit content was regarded as sufficient indication for additional administration of whole blood. If the hematocrit level rose or if the animal vomited, additional isotonic solution of sodium chloride was administered. Seven per cent gelatin was kept in readiness in case the hematocrit content continued to rise in spite of the administration of isotonic solution of sodium chloride. In some of the dogs occasional direct measurements of the systolic blood pressure were made.

In the 5 dogs receiving penicillin, the dosage for this drug was as follows: 100,000 units every two hours during the first twenty-four hours, beginning from between one-half hour to three hours postoperatively, 50,000 units every two hours during the next forty-eight hours and 50,000 units every two hours for the twenty-four hour period following the second operation. Thus the total dosage for each of these 5 dogs in the first twenty-four hours after the beginning of treatment was 1,200,000 units and by the end of the first seventy-two hours 2,400,000 units. The total dosage was 3,600,000 units in ninety-six hours. The relative magnitude of such a dosage schedule can be appreciated when it is pointed out that the weights for these 5 dogs averaged only a little over 33 pounds (15 Kg.). At autopsy on the control dogs, which was performed immediately after death, cultures were made, as mentioned, and the strangulated obstructed segment low in the ileum was removed, measured, photographed and then placed in solution of formaldehyde, along with sections of the major organs. This same procedure was followed in the penicillin-treated dogs at the operation for resection. Microscopic sections of tissues removed at autopsy were made, and bacterial stains were done on all sections of the intestine.

Blood specimens of all dogs were taken just before or immediately after death, for determinations of chloride and hematocrit levels. In addition, in some of the dogs other determinations such as the nonprotein nitrogen, total serum protein, calcium, phosphorus, sodium, potassium and carbon dioxide-combining power were made.

RESULTS

I. Control Dogs.—The survival time for the 5 control dogs ranged between twenty-six and a half hours and thirty-six hours (chart 1). The determinations of hematocrit levels and the fluids administered to each dog are plotted in table 1. A sixth dog, intended for the control series, showed at autopsy strangulation of the proximal turned-in end, with leakage of intestinal contents into the peritoneal cavity, and was excluded from the series. The symptomatology, which was the same in each of these dogs, has been described in detail.[8] Briefly, they were usually awake and standing in their cages in from two to ten hours; within four to sixteen hours postoperatively they had vomited bloody, foul-smelling material, which was at first bright red and later

a dark brownish red. The amount and severity of the vomiting varied, and the amount of isotonic solution of sodium chloride given subcutaneously varied accordingly. Ascites, which was always bloody at autopsy, became clinically evident within five hours after operation. Often large, distended loops of bowel were both palpable and visible beneath the wall of the abdomen. Borborigmi were audible and violent peristaltic movements visible. The animals died in a remarkable manner. In some cases they would appear to be in relatively good condition and would extend their legs, gasp and die. In other cases (3) there was a terminal "toxic" phase, lasting from twenty minutes to seventy minutes. This phase was marked by severe retching and vomiting while the dog was erect, followed by a slumping to the prone position. At this stage, all four legs were paralyzed and the animal would collapse if an attempt was made to stand it up. Soon the animal would become comatose, and it would die within a few minutes after extending its legs. In all animals death was rapid and not at all characteristic of the slow deaths of dogs dying in shock. In only 1 of the 5 dogs was a gross perforation of the strangulated bowel observed at autopsy, and this was through a large, round mucosal ulcer located on the mesenteric border of the bowel. This is in pronounced contrast to 10 controls reported on,[8] in 5 of which bowels were perforated, and in these the perforations were antimesenteric in location. The bowel contained old, foul-smelling blood in all cases. The peritoneal cavities contained between 500 and 2,000 cc. of bloody transudate having the composition of blood serum and a hematocrit level of around 15. The strangulated segments showed gross and microscopic evidence of ulceration, necrosis of the intestinal wall and pronounced hemorrhage into the wall. There was always pronounced ulcerative diphtheritic enteritis and also infection of the damaged and necrotic wall. Bacterial stains revealed the presence of many types of bacteria, both gram-positive and gram-negative, in the intestinal wall.

II. Dogs Treated with Massive Doses of Penicillin.—Of the 5 dogs treated with massive doses of penicillin included in this report, all lived seventy-two hours, at which time resection of the strangulated segment was carried out. There was a sixth dog treated with penicillin, which died in under twenty-nine hours and which at autopsy proved to have strangulation of the proximal turned-in end. This end leaked bowel contents into the peritoneal cavity, and as a result this animal was excluded from the series.

As is illustrated in the chart, 1 of the dogs died eight hours after resection of its strangulated bowel. This dog was "toxic" for perhaps an hour prior to operation. It was retching and vomiting strenuously, and it had a rapid thready pulse. At the time at which resection was performed the dog was still standing and had not yet become comatose.

After operation, which as in other dogs was performed with the animal under local anesthesia, the dog seemed better. However, it did not stand up, and eventually it died, without vomiting. At autopsy, the anastomosis was found to be perfectly satisfactory and there was no leakage of the suture lines. The other 4 animals subjected to resection were in relatively good condition at the time of operation, and all 4 were cured by this procedure. One of these (no. 95) was killed over a month postoperatively, and the other 3 dogs are still alive and well over a month postoperatively.

The strangulated obstructed segment of bowel resected in each dog resembled similar segments from control dogs in color, weight and length. None, however, were perforated. All showed the characteristic acute diphtheritic ulcerative enteritis, and all were distended with dark foul-smelling bloody material. Between 300 and 2,000 cc. of bloody peritoneal transudate was aspirated during operation. Isoperistaltic

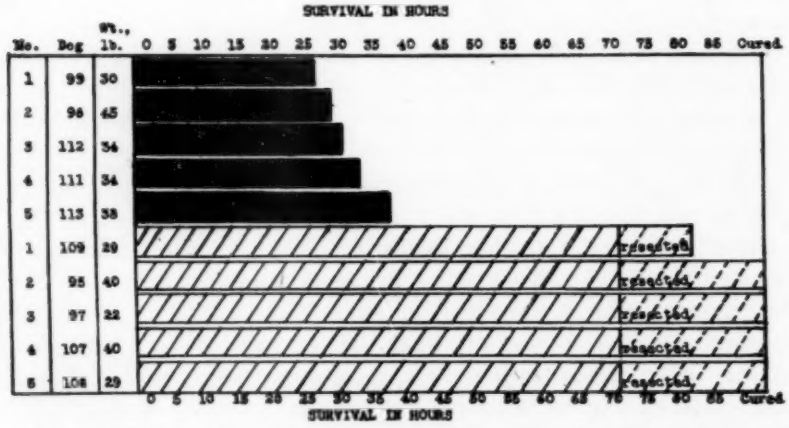

Chart 1.—The survival times of dogs with strangulated ileal obstructions treated with massive doses of penicillin in which resections were carried out at seventy-two hours as compared with the survival times of dogs with strangulated ileal obstructions not treated with penicillin. Both groups were treated for hemorrhage, shock and loss of chloride and water. Solid lines indicate the postoperative survival time of control dogs with strangulated ileal obstructions. The light shaded lines indicate the postoperative survival time of dogs with strangulated ileal obstructions treated with penicillin and in which resection was performed after seventy-two hours.

side to side anastomoses of the proximal part of the bowel above the resected strangulated segment to the distal segment below the distal turned-in end were used to reestablish the continuity of the intestinal tract. Usually within two or three hours after this had been done the animals passed tarry stools. There was no postoperative vomiting, and the animals seemed well within a few hours. These dogs were allowed small amounts of water within five or six hours, milk within twenty-four hours and solid food within seventy-two hours after operation. The

TABLE 1.—*Hematocrit Levels and Fluid Therapy After Production of Intestinal Obstruction and Strangulation*

Dog	Fluids Administered *	Control Dogs Hr. Postoperatively 0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	45	50	55	60	65	70	75	80	Total Fluid
96 (45 lb.)	Hematocrit level	47	...	48	...	43	49	...	...	...	...	41	...	41	...	41	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1,250 cc. of blood, 1,800 cc. of saline sol. in 28 hr.
	Blood, cc.	...	500	...	...	500	...	250	...	...	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	500	...	300	...	...	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
99 (30 lb.)	Hematocrit level	42	50	...	40	43	45	40	...	...	27	...	35	37	35	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1,200 cc. of blood, 250 cc. of plasma, 2,000 cc. of saline sol. in 26½ hr.
	Blood, cc.	...	500	...	...	500	...	...	...	...	...	...	200	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	500	...	...	500	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
						250 (plasma)																									
111 (34 lb.)	Hematocrit level	45	...	....	44	40	36	37	38	...	31	...	37	...	38	39	clotted		...	...	...	...	...	...	...	...	...	...	...	...	2,000 cc. of blood, 2,000 cc. of saline sol. in 32 hr.
	Blood, cc.	...	500	...	...	...	500	...	...	...	...	500	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	...	500	...	...	...	...	500	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
112 (34 lb.)	Hematocrit level	47	...	...	50	45	40	...	44	44	...	...	40	39	35	33	36	...	...	...	...	...	...	...	...	...	...	...	...	...	1,550 cc. of blood, 2,000 cc. of saline sol. in 29 hr.
	Blood, cc.	...	500	...	...	...	500	...	...	...	...	250	...	...	300	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	...	500	...	...	...	...	250	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
113 (38 lb.)	Hematocrit level	55	...	50	50	49	47	46	...	...	44	35	...	39	40	...	37	37	...	...	...	...	...	...	...	...	...	...	...	...	1,500 cc. of blood, 2,950 cc. of saline sol. in 36 hr.
	Blood, cc.	...	500	...	...	...	500	...	...	...	...	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	...	500	...	...	...	...	...	350	...	500	...	800	300	...	...	...	...	...	...	...	...	...	...	...	...	
		Penicillin-Treated Dogs †																													
95 (40 lb.)	Hematocrit level	42	...	42	...	...	40	38	38	...	...	31	...	...	31	...	34	35	...	34	33	36	...	32	34	35	...	37 resected			2,000 cc. of blood, 2,400 cc. of saline sol. in 72 hr.
	Blood, cc.	...	500	...	...	500	...	...	...	...	...	...	...	500	...	...	...	...	...	...	...	...	...	...	...	...	500	...	...		
	Saline sol., cc.	...	500	...	...	...	...	...	...	500	...	...	...	...	...	...	...	...	400	...	...	500	...	500	...	...	...	...	...		
97 (22 lb.)	Hematocrit level	46	...	41	...	...	42	...	45	61	...	...	36	...	43	...	39	37	...	34	...	34	34	51	28	32	...	38 resected			2,800 cc. of blood, 2,800 cc. of saline sol. in 72 hr.
	Blood, cc.	...	500	...	...	500	...	...	250	...	...	...	...	500	...	...	...	...	...	...	250	...	...	...	400	...	...	400	...	...	
	Saline sol., cc.	...	500	...	...	...	...	...	250	...	...	...	...	...	...	...	...	...	250	...	250	...	...	...	...	1,200	...	...	...	...	
107 (40 lb.)	Hematocrit level	51	...	...	...	45	40	45	...	...	...	46	...	40	...	41	...	...	36	...	...	...	...	32	39	40	44	32	50 resected		2,300 cc. of blood. 3,600 cc. of saline sol. in 72 hr.
	Blood, cc.	...	500	...	...	...	500	...	...	...	300	...	...	...	...	...	...	500	...	...	...	...	...	...	...	...	...	500	...	...	
	Saline sol., cc.	...	500	...	...	...	...	500	...	...	...	...	500	...	...	...	...	...	500	...	...	...	...	...	...	...	...	600	500	500 p.o.	
108 (29 lb.)	Hematocrit level	50	...	...	46	52	...	53	...	44	...	40	...	35	35	...	38	...	36	...	48	45	40	40	...	...	...	46 resected			2,450 cc. of blood, 3,300 cc. of saline sol. in 72 hr.
	Blood, cc.	...	500	...	...	...	...	...	300	250	...	...	...	400	...	500	...	...	...	...	...	...	500	...	...	...	...	...	...	...	
	Saline sol., cc.	...	500	...	...	...	...	...	500	...	...	...	500	...	...	...	...	...	500	...	...	...	...	...	300	...	500	500	...	...	
109 (29 lb.)	Hematocrit level	52	...	...	49	49	53	...	...	53	...	56	...	54	...	47	47	45	...	...	50	50	...	43	43	...	...	43 resected			1,100 cc. of blood, 4,300 cc. of saline sol. in 72 hr.
	Blood, cc.	...	500	...	...	...	...	...	...	...	...	...	...	300	...	...	...	...	...	...	...	...	...	...	...	...	...	300	...	...	
	Saline sol., cc.	...	500	...	...	...	...	...	...	...	...	...	...	500	...	...	500	...	...	...	500	...	500	...	500	300	500	500	...	...	

* Blood was administered intravenously, and isotonic solution of sodium chloride was given subcutaneously.
† After seventy-two hours of administration of penicillin, dogs were submitted to operation for resection.

determinations of hematocrit levels and the fluids administered to the dogs given penicillin and then resected are plotted in table 1. Microscopic sections of the strangulated bowel removed revealed necrosis and pronounced hemorrhage into the intestinal wall, ulceration and infection. Bacterial stains revealed the presence of many types of bacteria, both gram-positive and gram-negative. In many sections the number of bacteria was definitely less than in similar sections of strangulated bowel from control dogs.

CHEMICAL STUDIES

It was found, as was expected, that in the dogs which died there was terminally a rise in the serum nonprotein nitrogen. The values for phosphorus and potassium were high. The values for chloride and sodium were within the normal range or above it. The carbon dioxide values were low and indicated the presence of acidosis.

Bacteriologic Studies.—The organisms most frequently encountered in the intestinal tract were Escherichia coli, Streptococcus faecalis, Staphylococcus aureus and Clostridium welchii. Pseudomonas aeruginosa and Proteus vulgaris were also occasionally grown. Rarely one organism would overgrow the others to produce a pure culture. The peritoneal cultures were often sterile during the first twenty-four hours, whether or not the dogs were treated with penicillin, unless perforation had occurred.[8] All specimens of heart blood in this series were sterile.

TABLE 2.—*Fluid Therapy in Paired Dogs over Equal Units of Time*

The total fluids for the control dogs during their survival and the fluids given corresponding penicillin-treated dogs (see table 1) for comparable periods are listed. The dogs were paired thus: 96 and 95, 99 and 97, 111 and 107, 112 and 108 and 113 and 109.

	Five Control Dogs	Five Treated Dogs
Blood	7,750 cc.	7,300 cc.
Isotonic solution of sodium chloride	10,750 cc.	6,250 cc.
Total	18,400 cc.	13,550 cc.

The Factor of Shock.—There was often a diminution in the systolic blood pressure, but it is believed that no dog in this series died of shock. This subject was discussed fully previously.[8] It can be seen in table 2 that the control dogs were treated as vigorously for shock, hemorrhage, chloride and loss of water as were the penicillin-treated dogs.

COMMENT

Great strides have been made in reduction of the mortality rate associated with acute intestinal obstruction. This mortality rate has been brought down from around 60 per cent [9] to as low as 15 to 20 per

9. Miller, C. J.: Study of Three Hundred and Forty-Three Surgical Cases of Intestinal Obstruction, Ann. Surg. **89**:91-107 (Jan.) 1929.

cent.[10] In one recent series [11] the mortality rate was reported to be 8 per cent. The chief factors responsible for this improvement, aside from more modern surgical technic and better methods for the management of shock, were the introduction of methods for the relief of distention by intubation and suction [12] and advances in knowledge concerning electrolyte and water balance.[13]

This progress, although representing a great victory in the treatment of an important surgical condition, has not yet reached a point where the results of treatment can be regarded with complacency. The so-called conservative school of management of intestinal obstruction is represented by surgeons who prefer to try to differentiate on clinical evidence between strangulated and nonstrangulated obstructions. This is done so that operation may be delayed in the cases of nonstrangulated obstruction for purposes of decompression and replacement of fluid. Those who adopt such a conservative regimen must not overlook the fact that early strangulation is difficult if not impossible to diagnose accurately short of direct visualization of the affected bowel wall. Furthermore, the factor of strangulation is the most important single factor in determining the outcome of a case of acute obstruction.[14] Because of the efficacy of penicillin in experimental strangulated obstructions,[8] a trial of massive doses of penicillin has been advocated by Calihan,

10. Calihan, R. J.; Kennedy, J. D., and Blain, A., III: Intestinal Obstruction: A Study of Two Hundred and Four Acute Cases with Reference to the Possible Efficacy of Anti-Bacterial Therapy, Bull. Johns Hopkins Hosp. **79**:21-33 (July) 1946.

11. Moses, W. R.: Acute Obstruction of the Small Intestine: A Report of One Hundred and Eighteen Cases, New England J. Med. **234**:78-81 (Jan. 17) 1946.

12. Abbott, W. O., and Johnston, C. J.: Intubation Studies of the Human Small Intestine, Surg., Gynec. & Obst. **66**:691-697 (April) 1938. Johnston, C. G.: Decompression in the Treatment of Intestinal Obstruction, ibid. **70**:365-367 (Feb.) 1940. Wangensteen, O. H.: Intestinal Obstructions. ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1942.

13. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, J. A. M. A. **59**:82-87 (July 13) 1912. McLean, A., and Andries, R. C.: Ileus Considered Experimentally, ibid. **59**:1614-1617 (Nov. 2) 1912. Haden, R. L., and Orr, T. G.: Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, J. Exper. Med. **38**:55-71 (July) 1923. MacCallum, W. G.; Lintz, J.; Vermilye, H. N.; Leggett, T. H., and Boas, E.: The Effect of Pyloric Obstruction in Relation to Gastric Tetany, Bull. Johns Hopkins Hosp. **31**:1-7 (Jan.) 1920. Coller, F. A.; Bartlett, R. M.; Bingham, D. L. C.; Maddock, W. G., and Pedersen, S.: Replacement of Sodium Chloride in Surgical Patients, Ann. Surg. **108**:769-782 (Oct.) 1938.

14. McKittrick, L. S., and Sarris, S. P.: Acute Mechanical Obstruction of the Small Bowel: Its Diagnosis and Treatment, New England J. Med. **222**:611-622 (April 11) 1940. Calihan and others.[10]

Kennedy and Blain [10] in an attempt to further reduce the attendant mortality in cases of acute mechanical intestinal obstruction. The experiments reported here, in which massive doses of penicillin prolonged the lives of animals with strangulated obstructions to a point which was twice the survival of untreated controls and at which time successful resections were performed, are not intended to encourage delay in operation for acute intestinal obstruction. They are presented, in the first place, as evidence of the great importance of bacterial infection in determination of the outcome of strangulated intestinal obstruction and, in the second place, to demonstrate the value of the preoperative use of massive doses of penicillin in experimental strangulated obstructions.

CONCLUSIONS

1. Massive doses of penicillin prolong the lives of experimental animals with strangulated ileal obstructions as compared with untreated controls when in both groups, shock, hemorrhage, chloride and loss of water are combated.

2. After a period twice as long as the survival time of the controls, the strangulated bowel was resected in 5 penicillin-treated dogs, with complete recovery in 4 of these dogs.

3. Therapy with massive doses of penicillin is recommended in all cases of acute intestinal obstruction in which strangulation is believed to be present or in which strangulation cannot be ruled out. This should be an adjunct to and not a substitute for early operation in such obstructions.

AIR FORCE BATTLE CASUALTIES

An Experience with Acute Injuries of Eight Hundred and Thirty-Nine Battle Casualties from the Eighth Air Force

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AIR FORCE crews in combat are subject to injury not only from enemy gunfire but also from the effects of cold or anoxia at high altitudes, from burns or injury from crash landings or parachute jumps or from a bizarre assortment of accidents within a plane in flight, the commonest of which is being caught in a moving gun turret.

During the course of the year March 1, 1944 to March 1, 1945, 1,054 battle casualties from the Eighth Air Force were admitted to the Sixty-Fifth General Hospital, located at Redgrave Park, Suffolk, England. Two hundred and fifteen of these were admitted as transfers from station hospitals in the vicinity. Eight hundred and thirty-nine were admitted to this hospital for definitive care, directly from their bases, on an average of five and one-half hours after being wounded. The latter group, of 839 patients, forms the basis of this report.

During the course of the year covered by this study there were 6,816 patients admitted to the surgical service, of whom 4,072 were admitted directly from Air Force units. Fifty-four per cent of these Air Force personnel were admitted for surgical diseases, 25 per cent for non-battle-injuries and 20 per cent for battle casualties, the last of which are the subject of this report. The Air Force battle casualties comprised 12.3 per cent of the total patients admitted to the surgical service for the year.

According to Army directives, injuries which occur during the course of a combat mission are classified as battle casualties. Those caused by direct enemy action are designated as battle wounds and those by accident in combat as battle injuries. Of the 839 patients with acute injuries, 645 had battle wounds from missiles, 140 battle injuries from plane crashes, 26 battle injuries from parachute jumps and 28 injuries from plane accidents (table 1).

The patients were members of sixty-six different bomber or fighter groups. The largest number from any one group was 92. Thirteen groups sent over 20 patients each. All casualties except 29 were from heavy bomber groups. The largest number of fresh casualties to arrive

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in any one day was 24. On only nineteen occasions were 10 or more casualties received in any twenty-four hour period.

ANALYSIS OF 645 CASUALTIES INJURED BY MISSILES

As shown in table 1, of the acute battle wounds from missiles, five hundred and forty-four were caused by flak, fifty-four by 20 mm. cannon shell, twenty-eight by secondary missiles set in motion usually by flak, fourteen by machine gun shells, three by rifle bullets, one by a rocket and one by bomb fragments. The low proportion of wounds from 20 mm. cannon shell in comparison with those in statistics compiled by the Fifteenth Air Force [1] and by the Eighth Air Force [2] during an

TABLE 1.—*Analysis of Cause of Injury in 839 Battle Casualties*

Battle casualties with acute injuries			839
From missiles		645	
Flak	544		
Cannon shell	54		
Secondary missiles	28		
Plexiglass	25		
Plane parts	2		
Oxygen bottle	1		
Machine gun shell	14		
Rifle bullets	3		
Rocket	1		
Bomb	1		
From crash		140	
From parachute jump		26	
From plane accidents		28	
Caught in turret	11		
Foot	2		
Arm	3		
Head	3		
Thorax	3		
Cold injury	3		
Falls	2		
Hit by dropping bombs	2		
Burns	2		
Anoxia	1		
Struck by prop	1		
Sprained shoulder throwing chaff	1		
Lung irritation from smoke	1		
Hand injury cleaning gun	1		
Foot injury from floor plate	1		
Hand injury in crank	1		
Face injury from nose wheel	1		

earlier period is explained by the reduction in enemy fighter opposition during the period of this study.

Table 2 shows the location of the eight hundred and sixty-three wounds which occurred in the 645 casualties injured by missiles. Sixty-nine per cent of these wounds occurred in the extremities, 11 per cent in the trunk and 20 per cent in the head and neck. Of the wounds of the extremities fractures occurred in 25 per cent, neural injuries in 8 per cent, and major arterial injuries in 5.5 per cent. Of the wounds

1. Benson, O. O., Jr., and Hoffman, I. L.: A Study of Wounds in Combat Crews, Air Surgeon's Bull. **1**:1 (July) 1944.

2. MacFee, W. F.: The Treatment of Air Force Combat Casualties, Ann. Surg. **120**:1 (July) 1944.

of the trunk 40 per cent resulted in visceral penetration. Six additional patients, with wounds of entrance in the neck or extremities, had injuries within the thoracic or the peritoneal cavity.

Table 3 shows the distribution of the 645 men wounded by missiles according to the position of their major injury. The number of craniocerebral and thoracic injuries is disproportionately high because patients

TABLE 2.—*Location of the 863 Wounds Occurring in the 645 Patients Injured by Missiles*

Region	Location	Number	Per Cent	Region	Location	Number	Per Cent
Head and neck, 20 per cent	Head	57	6.6	Upper extremity, 28.8 per cent	Shoulder	51	5.9
	Face	52	6.0		Arm	77	8.9
	Eye	44	5.1		Forearm	61	7.0
	Neck	20	2.3		Hand	61	7.0
Trunk, 11 per cent	Thorax	43	5.0	Lower extremity, 40 per cent	Thigh	170	19.7
	Abdomen	14	1.6		Leg	137	15.9
	Lumbar region	6	0.6		Foot	37	4.3
	Buttock	33	3.8				

with serious injuries of the head and chest from station hospitals in the vicinity, also serving the Air Forces, were sent immediately to this hospital. The low incidence of penetrating thoracic and abdominal wounds as compared with wounds of ground forces in the field [3] is attributed to the effectiveness of body armor worn by crews of heavy bombers in combat. Grow and Lyons [4] have demonstrated a 58 per cent reduction in thoracic wounds and a 36 per cent reduction in abdominal

TABLE 3.—*Distribution of Casualties According to Structures Injured in 645 Fresh Battle Wounds from Missiles*

Location	Cases	Per Cent
Soft parts	373	57.8
Skeletal system *	164	25.4
Eye	38	5.9
Craniocerebral region	25	3.8
Abdominal region	18	2.8
Faciomaxillary region	14	2.2
Thoracic region	13	2

* Not including head, face or thorax.

wounds in crews of bombers of the Eighth Air Force after the introduction of body armor.

Of 645 airmen wounded by missiles the positions flown by 530 in heavy bombers were recorded. These data are presented in table 4.

3. Hoche, O.: Die wehrchirurgische Behandlung der Verwundeten, Med. Klin. **35**:1532, 1939; Bull. War Med. **1**:1 (Sept.) 1940.

4. Grow, M. C., and Lyons, R. C.: Body Armor: A Brief Study of the Development, Air Surgeon's Bull. **2**:8 (Jan.) 1945.

TABLE 4.—*Analysis of Injuries in Crews of Heavy Bombers According to their Position in Plane*

Position in plane	Pilot		Co-pilot		Navigator		Bombardier		Radio Man		Ball Turret Gunner		Top Turret Gunner		Waist Gunner (2)		Tail Gunner	
Number airmen injured	37		29		60		84		50		42		33		135		60	
Total wounds	48		34		85		118		68		50		40		182		82	
Location of Wounds	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Head	3	29	1	12	3	23	6	24	7	20	1	14	2	17	15	19	8	16
Face	7		2		9		7		6		1		1		9		1	
Eye	1		2		4		10		1		5		1		8		3	
Neck	3		0		4		5		0		0		3		3		1	
Shoulder	2	31	3	30	7	39	7	36	3	25	2	22	4	22	11	27	4	29
Arm	7		3		5		14		5		5		4		21		6	
Forearm	2		9		11		10		6		2		0		8		7	
Hand	4		1		10		11		3		2		1		9		7	
Chest	2	4	4	15	7	13	8	9	6	15	2	10	1	5	5	12	1	12
Abdomen	0		1		2		0		0		1		0		5		2	
Lumbar region	0		0		1		1		2		0		0		3		1	
Buttock	0		0		1		2		2		2		1		11		6	
Thigh	10	35	7	42	11	24	15	31	14	40	15	54	11	55	46	41	18	42
Leg	6		4		9		18		9		10		10		22		15	
Foot	1		3		1		4		4		2		1		6		2	

The incidence of injures in pilots, co-pilots and turret gunners was somewhat lower than in those flying other positions. The table does not show any significant difference in the location of wounds according to the position flown in the plane.

Treatment of injured air force casualties was begun by the crew in the plane before it landed. The presence of mind of these men and their efficiency in caring for fellow crew members spoke well for their training and equipment. The readjustment of oxygen masks and oxygen supply, application of pressure bandages to control hemorrhage, closure of sucking wounds of the chest by appropriate dressings, relief of pain by morphine and application of warmth were all done effectively by these men working under the adverse conditions of flight at high altitude.

When the aircraft landed at its base a wounded man was first seen by his flight surgeon. If he were seriously wounded or had a fracture of a long bone, his removal from the plane was often difficult. It was accomplished with greatest ease and least harm to the patient by first wrapping him in a Neil Robertson litter (fig. 1). He then usually remained in this litter until he was put on the operating table at the hospital.

From the plane an injured airman was first taken to the medical station on the field where he landed. Here the first aid measures begun on the plane were checked and continued, and plasma was given if necessary to restore blood pressure. Prolonged efforts to combat shock were not advisable at the base, and, after several bottles of plasma had been given, if the condition was not much improved the administration of plasma was continued in the ambulance and the patient brought on to the hospital.

Resuscitation and Triage.—At the hospital, casualties were received in the shock ward, where they were placed on a bed without first being removed from the stretcher or Neil Robertson litter. Those with wounds of the head or chest were placed with the head of the bed elevated 8 inches (20 cm.). Others were placed with the head lowered a similar distance. In the shock ward the blood pressure and pulse were taken, general condition appraised, shock combated, clothes removed (usually by cutting them off), wounds inspected and a rapid but complete examination done, particular attention being paid to possible injuries of nerves, bones, tendons or blood vessels in wounds of extremities and to the possibility of thoracic or abdominal penetration in all wounds over the trunk, shoulders, neck, buttocks or upper part of the thighs. A history of the injury and description of the physical findings was recorded, roentgenograms of the affected part taken, preoperative medication given (usually 1 cc. of tetanus toxoid and 0.6 mg. of atropine) and the skin surrounding the wound shaved. This was done, more or less in the order as given, prior to removal to the operating room.

Roentgenograms of all casualties were taken before operation. My colleagues and I have seen a patient in whom a piece of flak entered the shoulder below the level of the insertion of the deltoid and lodged in the lower lobe of a lung. In another patient the missile entered the lateral surface of the thigh at the junction of the middle and lower third and lodged in the bladder. Frequently missiles entering the buttock penetrated the peritoneal cavity or injured the rectum below the pelvic floor. For this reason roentgenograms of a large area of the body, including anteroposterior, lateral and often oblique views, were necessary if the true nature of the wound were to be recognized.

Shock was treated with transfusions of whole blood. While plasma was undoubtedly of great value in the first aid treatment of shock, it

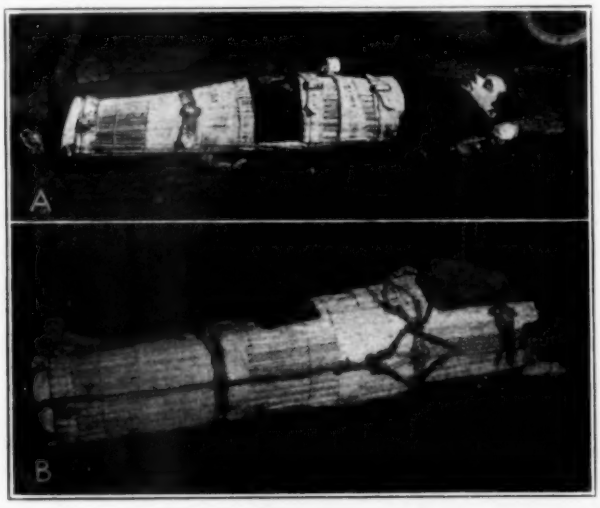

Fig. 1.—*A*, the Neil Robertson litter, used in removing casualties from the plane and in transporting them to the hospital. *B*, another view of the Neil Robertson litter, showing its under surface.

had little place in its management in the hospital. Large transfusions were often necessary, and we have frequently given 8 or 10 bottles of blood before and during operation. This blood was supplied through our own blood bank, from donors in our detachment and from the air fields.

Warmth was supplied only by the application of blankets. Oxygen was available at all beds in the shock ward. It was given to the patients with thoracic injuries and occasionally to those in shock. Adrenal cortex extract has not been used. Morphine had usually been given by crew members or at the base, and further administration was rarely necessary.

The copper sulfate method of estimating values for specific gravity of blood and plasma was employed. From these figures the estimation

of hemoglobin, hematocrit and plasma protein levels was calculated, and the results were used in determining the therapy for most of the patients with shocking injuries. The procedure was of most value in following the hemoconcentration of burns. In a patient who had suffered a traumatizing injury with loss of blood and had in addition received plasma at his base before being brought to the hospital, the information which it supplied was often not of great value. We preferred to estimate the degree of shock from a general clinical appraisal of the condition rather than from any one laboratory aid.

If concealed hemorrhages were suspected, we did not hesitate to begin operation on any patient as soon as he had received rapidly several bottles of blood and had an intravenous cannula in place, with blood running into the vein smoothly. In all others we preferred to wait until recovery from shock had begun. The administration of blood was continued during operation in all patients who had been in shock or in whom the development of shock was anticipated.

Reactions to transfusions had to be guarded against. The use of transfusions of 2, 3 or 4 liters of blood to combat shock and to help sustain a patient through the prolonged and ofttimes traumatizing operation necessary to repair the damage of war injuries has been one of the major developments in the surgical therapy of this war. However, hemolytic reactions to transfusions are probably more prone to follow these large, multiple or repeated transfusions. Hemoglobinuric nephrosis with uremia was the cause of death in 1 of the 3 patients dying from missile wounds in this series. It also developed following transfusion in 2 injured men before they were transferred to us from station hospitals. They are not included in this series of acute injuries in battle casualties. In an airman with a third degree burn of 65 per cent of his body surface, incurred after a crash landing, a similar condition was found at autopsy.

Alkalinization of the urine was carried out in an endeavor to prevent the renal damage resulting from hemoglobinemia and hemoglobinuria. In cases of elective transfusions this was routinely carried out by the giving of sodium bicarbonate or sodium citrate by mouth before the transfusion was given. In cases requiring large transfusions as an emergency measure, an additional 1.25 Gm. of sodium citrate intravenously was given with each bottle of blood and, if a reaction occurred, at two hour intervals until the urine was alkaline or was free of hemoglobin.

Wounds of the soft parts, not including visceral penetrations, accounted for 373, or 57 per cent, of the patients with battle wounds from missiles. These wounds were treated by excising all devitalized tissue, removing foreign bodies, irrigating with isotonic solution of sodium chloride, dusting lightly with sulfanilamide powder in most of

the cases (average 5 Gm. per patient), inserting loosely a gauze strip covered well with petrolatum to the depth of the wound and applying a voluminous dressing snugly. Forceful packing of a wound was not done. Ample incisions through skin and fascia along the natural lines of skin cleavage are necessary for adequate exposure. Transverse incisions in the extremities are not advised.

The extent of the débridement was dependent on the nature of the wound. In some wounds, where the missile struck at high velocity, a wide excision of traumatized tissue was necessary. In others, caused by missiles of low velocity, little damage was done and a minimal excision of the entire wound was necessary. Usually the débridement had to be done in layers as the various tissue planes presented. Only rarely was en bloc excision of the entire wound possible. Most wounds had portions of woolen flying suit along the tract, and often wool was wrapped around the missile. For this reason effort was made to remove all foreign bodies. This was usually not difficult, as the wound tract could be followed to the missile. Small fragments of shells often could not be easily located, and, if in a position where their presence would cause no harm, no prolonged search was made for them.

Sulfanilamide crystals were lightly dusted into the wounds of about 80 per cent of the patients. Except for an increased discharge of tissue fluid and blood from the wounds, no harm was noted from its local use in wounds left open for later secondary suture. In the group of patients in whom it was not used there was no essential gross difference in healing of wounds from the healing in treated patients.

Sulfadiazine was given routinely by mouth until after secondary closure of the wound had been done. When penicillin became readily available it was given in doses of 20,000 units every three hours for four or five days to patients with major wounds. Pentothal sodium was the anesthetic agent used in most cases, although some débridements were done under regional block or direct infiltration of procaine hydrochloride.

Wounds in the scalp, face and all serous cavities were closed after excision. All others were left open and not dressed until five days later, when the patient was returned to the operating room, dressings and petrolatum gauze removed and secondary closure done. If secondary closure was impossible because of the size of the wound, grafting with split thickness skin grafts was done at the time (figs. 2, 3 and 4).

Wounds of the skeletal system, not including ribs or bones of the face or skull, were present in 164, or 25 per cent, of the patients with battle wounds from missiles (table 3). Bones involved are shown in table 5. In their care the wounds of the soft parts were débrided as described. All loose fragments of bone were removed. The wounds were then irrigated with isotonic solution of sodium chloride and lightly dusted with sulfanilamide, and petrolatum gauze was inserted loosely.

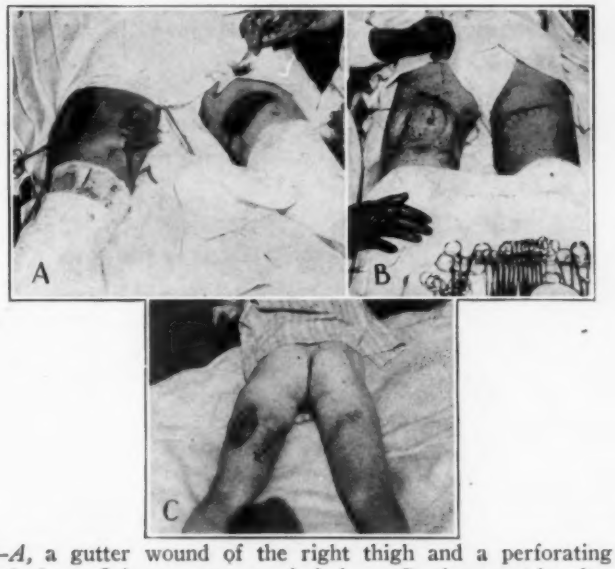

Fig. 2.—*A*, a gutter wound of the right thigh and a perforating wound of the left thigh from flak as seen on admission. *B*, the wounds after secondary closure and grafting, five days later. *C*, complete healing after fourteen days.

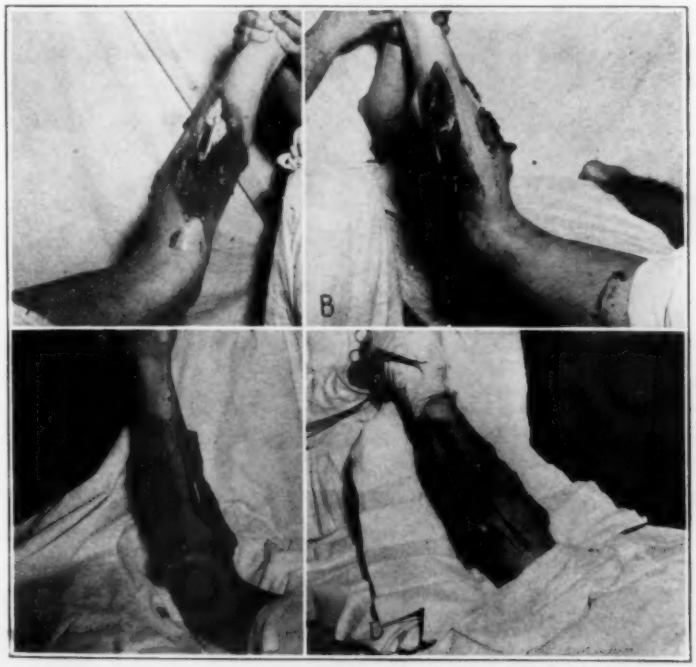

Fig. 3.—*A*, a perforating wound from flak through the leg as seen on admision. *B*, patient viewed from the opposite side. *C*, wounds on removal of dressings, five days after débridement. *D*, wounds after application of split thickness grafts on the same day.

In cases of injuries of the long bones requiring traction to maintain bone length, skeletal traction was then applied. In all others and in

Fig. 4.—Same patient as in figure 3, showing complete healing.

TABLE 5.—*Bones Involved in 164 Cases of Wounds from Missiles with Skeletal Injury*

Location	Number	Bones
Long bones	3	Radius and ulna
	6	Radius alone
	15	Ulna
	23	Humerus
	22	Femur
	4	Tibia and fibula
	18	Tibia alone
	16	Fibula alone
Hands and feet	11	Phalanges of the hand
	12	Metacarpals
	6	Carpals
	8	Tarsals
	5	Metatarsals
Miscellaneous	5	Scapula
	6	Pelvis
	3	Patella
	2	Vertebra
	2	Elbow joint
	2	Knee joint
Amputations (immediate)	3	Thigh
	4	Leg
	1	Foot
	4	Toes
	2	Fingers

injuries of the long bones, where damage to muscle was so extensive or loss of bone so pronounced that traction was not necessary, well padded plaster casts were applied. Shattering of bone was often exten-

sive (fig. 5). Internal or external skeletal fixation was not used. The first dressings were done in the operating room five days after débridement, at which time the wounds were closed if possible by suture or skin graft.

Wounds penetrating the skull or brain occurred in 25, or 3.8 per cent, of the 645 casualties injured by missiles. Sixteen of these were penetrating wounds of the skull and brain, usually with indriven fragments of bone, while 9 resulted in fractures of the skull, usually depressed, without dural penetration. In all cases the scalp was débrided, loose fragments of skull removed, the defect of the skull enlarged, traumatized

Fig. 5.—Roentgenogram of a leg after a wound from flak, showing the typical comminution of a bone which occurs when it is struck by missiles of high velocity.

brain removed by suction and especial care taken to remove indriven fragments of bone. Bleeding was painstakingly controlled by coagulation or with silver clips and, in cases of venous sinus tears, by muscle packs or fibrin foam. In cases of penetrating wounds, dural grafts from temporal fascia, periosteum or fascia lata were usually necessary. If the defect of the bone was not repaired with a tantalum plate immediately, tantalum foil was usually placed between the scalp and dura to make subsequent plating easier. The wounds of the scalp were always closed.

Of these 25 patients, 1 with an extensive penetrating craniofacial wound from a 20 mm. cannon shell died (mortality 4 per cent). All the others made good recoveries. All except 1 were ambulant on dis-

charge. Four patients returned to duty. The others were returned to the United States.

Thoracic injuries occurred in 13, or 2 per cent, of the patients wounded from missiles. In none of these patients did the missile traverse the flak suit. In 1 the suit was not worn. In 1 the missile entered under the suit. In 5 the penetration occurred in the lateral unprotected portion of the chest, between the anterior and posterior axillary lines. In 4 the missiles entered through the shoulder and in 2 through the neck (fig. 6). We are convinced that the body armor

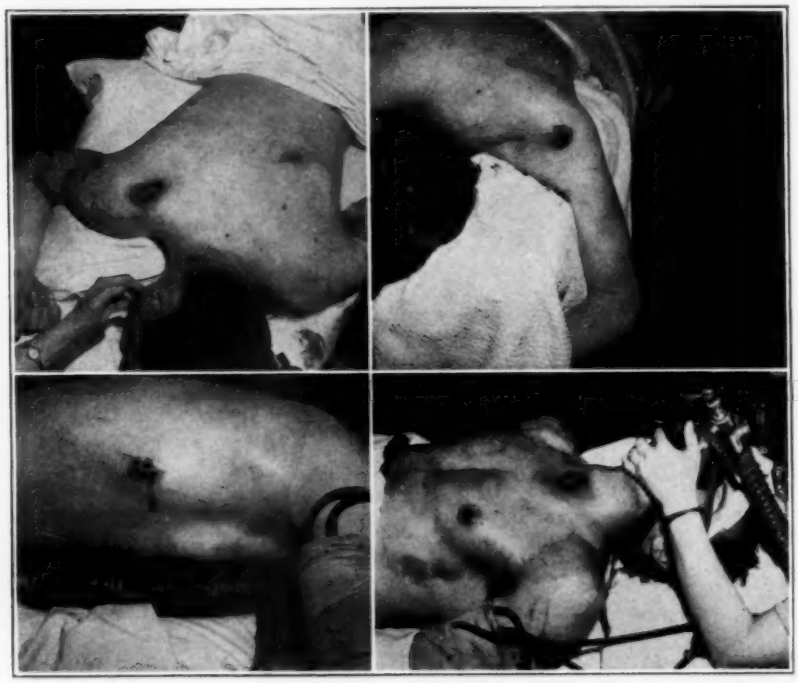

Fig. 6.—Four casualties with flak wounds of the chest, showing typical sites of penetration through shoulder, neck or lateral surface of the thorax. The chest is protected anteriorly and posteriorly by body armor worn by air force crews in combat.

worn by crew members of heavy bombers has greatly reduced the incidence of thoracic wounds.

Penetrating wounds occurred eight times, the missiles lodging in the lung in 4 patients, in the mediastinum in 2 and in the opposite thoracic wall in 2. In 2 patients the missile traversed the lung and both walls of the thorax, in 1 of these patients also going through the dome of the diaphragm and the right lobe of the liver. Tangential sucking wounds with shattered ribs but without penetration of the lung occurred in 3 cases.

Thoracotomy with the patients under ether administered endotracheally as soon as they could be prepared for operation was done in all except 1 case in which a tiny fragment from a 20 mm. cannon shell had lodged in the lung and no operation was necessary. The missiles were removed in all the other cases.

The thorax was opened through the wound of entry in all cases except those in which the missile entered through the apex, in which cases an anterior approach through the third interspace was used. The wounds of the soft parts of the chest were débrided, the shattered rib fragments removed, particular care being paid to the removal of fragments driven into the lung or pleural cavity, the foreign body removed, the wound in the lung closed with sutures, the blood removed from the pleural cavity and the wounds of the soft part of the chest, exclusive of skin and subcutaneous tissue, closed without drainage. At the close of the procedure air was removed from the pleural cavity with a catheter or needle and 100,000 units of penicillin introduced. Thereafter daily thoracentesis was done until the chest was dry and the lung reexpanded.

There were no deaths in this series of patients with thoracic injuries. Empyema developed in 1 patient and was treated by drainage by catheter and rib resection. In 1 patient, with perforation of two lobes of the lung, reexpansion of the lung was not complete when the patient was evacuated to the United States. In another, in whom ligation of the subclavian artery just above the aorta was necessary, a partial clotted hemothorax was present when the patient was evacuated. Decortication was not done because of the development of jaundice in this patient. In all other patients complete restoration of function occurred in the damaged lungs.

Abdominal injuries requiring laparotomy occurred in 18, or 2.8 per cent, of the patients injured by missiles. The viscera damaged are shown in table 6. Ether administered endotracheally was the anesthetic used in each case. Perforations of the stomach and small intestine (fig. 7) were closed. In 1 case four complete end to end anastomoses were necessary in the small intestine. In colonic injuries the colon was extraperitonealized as a colostomy. Splenectomy was done for the one ruptured spleen. Cholecystectomy was performed for the perforated gallbladder. The pancreatic wound was drained, and the resultant pancreatic fistula closed spontaneously in a month. The wounds of the bladder were closed about a suprapubic catheter. A loop colostomy and perineal drainage of the perirectal tissues were done for the penetrating wound of the sacrum with perforation of the extraperitoneal portion of the rectum. Exploratory laparotomy and suprapubic cystotomy were done for the perineal wound with laceration of the urethra.

Two of these 18 patients died (mortality 11 per cent). One, in whom a large shell fragment had traversed the iliac bone, small intestine

and colon, died in twenty-four hours, with high temperature, stupor and hemiplegia from fat embolism of the brain. Another, with compound fractures of the humerus and femur and a penetrating abdominal wound with perforation of the gallbladder, in whom repeated blood transfusions were necessary, died eighteen days later, in uremia. The kidneys

Fig. 7.—A penetrating abdominal wound in the left flank, with evisceration of small intestine. There were numerous perforations of the descending colon and small intestine and one of the bladder. The missile lodged in the right thigh. The wound of entrance is in a part of the abdomen unprotected by the flak suit.

showed the typical changes of hemoglobinuric nephrosis. All other patients made good recoveries. All colostomies were closed. Eight patients were returned to duty and 7 evacuated to the United States.

Injuries to the eyes occurred in 38 patients as the primary cause for admission. In 6 others injuries of the eyes occurred as incidental

TABLE 6.—*Location of Wounds in 18 Cases Requiring Laparotomy Following Injury by Missiles*

Number	Location
3	Retroperitoneal hematoma
2	Herniated omentum
2	Small intestine (multiple)
2	Small intestine and colon (multiple)
1	Small intestine, colon and bladder
1	Gallbladder, liver, pancreas and stomach
1	Stomach and liver
1	Liver
1	Bladder
1	Spleen
1	Gallbladder
1	Rectum and ureter
1	Urethra

findings. There were intraocular foreign bodies in sixteen instances, foreign bodies in the cornea or conjunctiva in sixteen, rupture of the globe in three, lacerations of the cornea in eleven and intraocular hemorrhage in two. Six enucleations were necessary. Intraocular foreign bodies were removed in 8 cases.

Faciomaxillary injuries occurred in 14 cases. The maxilla was penetrated eight times and the nose twice, and in seven instances the

mandible was fractured. Wounds of the soft parts were débrided, with care not to sacrifice skin of the face unnecessarily. Wounds were then closed by primary suture. Fractures of the mandible were reduced and immobilized by intramaxillary multiple loop wiring with intermaxillary elastics for fixation by members of the dental service. Penetrating wounds of the maxilla were usually drained through a nasoantral window after débridement of bone fragments.

In 1 case a shell fragment penetrated the neck and pierced the hypopharynx. It was removed on laryngoscopic examination from the interarytenoid fold. The wound in the neck was explored, the injury to the hypopharynx débrided and closed and a tracheotomy done. The tracheotomy tube was removed in four days and the secondary closure done on the wound of the neck on the fifth day. Recovery was uneventful.

Injuries to the peripheral nerves occurred in 48 patients. The distribution of these cases is shown in table 7. Because of difficulty in

TABLE 7.—*Nerves Injured in 645 Battle Casualties Wounded by Missiles*

Immediate amputation was done in the case of the median and ulnar lesion and 3 cases of sciatic lesions.

Number	Nerve	Number	Nerve
1	Brachial plexus	9	Sciatic
1	Median and ulnar	6	Tibial
6	Median	3	Peroneal
9	Ulnar	1	Facial
9	Radial	1	Digital
1	Axillary	1	Plantar

detecting how widely a divided nerve is traumatized by shell fragments at the time of the original excision of the wound, nerve suture was rarely done until three weeks after the wound had been closed by secondary suture or graft. At this time the tantalum wire suture technic with tantalum foil cuff, as introduced by Col. R. Glenn Spurling, was used.

Arterial injuries occurred in 35 patients with injury due to missiles (table 8). In all cases bleeding had stopped by the time the patients arrived at the hospital, either because of arterial spasm, intravascular thrombosis or the presence of retained extravascular clots or because of a combination of these factors. Loss of blood had been severe in some, and transfusions were necessary in most of the cases. Direct visualization of the damaged artery with adequate exposure was necessary for proper management of the vessel without damage to the adjacent nerves. Temporary control of the bleeding artery was obtained by tourniquet or direct digital pressure on the bleeding vessel or by a tape placed about the artery above the injury. Vessels were ligated with either surgical gut or silk and were transfixed. Ligation in con-

tinuity of an artery was not done. The accompanying vein was ligated whenever a major artery was tied off.

Immediate amputation was done in three of the femoral, two of the popliteal and one of the radial and ulnar lesions, because of extensive injuries to the extremity. Gangrene of the foot subsequently developed in the external iliac lesion and of the foot and leg in one of the femoral and the remaining three popliteal injuries, necessitating amputation. Of these delayed amputations gas gangrene developed in the femoral and one of the popliteal injuries and hastened the removal of the leg.

Arterial suture was done five times, once in the common carotid artery, twice in the popliteal artery, once in the femoral artery, at the level of the entrance of the artery into the adductor canal, and once in a radial artery, where it was necessary to ligate the ulnar artery. Heparin was not available in any of the cases. Thrombosis occurred at the site of both popliteal sutures, collateral circulation was not sufficient to maintain the life of the extremity and amputation was neces-

TABLE 8.—*Major Arteries Involved in 645 Casualties Injured by Missiles*

Immediate amputation was necessary in 3 cases of femoral, 2 of popliteal and 1 of radial and ulnar lesions because of extensive injury to the extremities.

Number	Artery	Number	Artery
1	Common carotid	1	External iliac
1	Internal maxillary	6	Femoral
1	Costocervical trunk	2	Profundus femoral
1	Subclavian (mediastinal)	5	Popliteal
2	Brachial (upper third)	9	Posterior tibial
1	Brachial (at elbow)	3	Peroneal
2	Radial and ulnar		

sary. Adequate circulation was maintained after the other arterial sutures.

Secondary hemorrhage or the development of an aneurysm did not occur in any of these cases. In 1 case an unrecognized injury to a posterior tibial artery resulted in an aneurysm, which was later excised. In another case, in which an injury to the posterior tibial artery was recognized and the vessel ligated, secondary hemorrhage occurred on the twelfth day from an injured peroneal artery which was not recognized at the time of the original débridement. The bleeding peroneal artery was located and ligated without disturbing the viability of the limb.

Bacterial Flora.—Débrided tissue was cultured in 177 cases. Organisms of the Clostridium group were present in 73, or 41.2 per cent, of the cases. Of these Cl. welchii was present thirty-eight times, Cl. oedematiens eleven, Cl. septicum eighteen, Cl. sporogenes nine, Cl. histolyticum nine, Cl. tertium four and Cl. tetanomorphum, Cl. tetani and Cl. fallax once each. Staphylococcus aureus was present one hundred and fifty-four times, in forty-seven of which the organisms were hemo-

lytic. Streptococci were present in 98 cases. In 14 of these the organisms were hemolytic and in 39 anaerobic. Organisms of the coliform group were present in only 4 cases.[5] This bacteriologic flora is essentially the same as that found in civilan wounds by Altemeier and Gibbs.[6]

Infection with Cl. welchii occurred in 2 patients. In a femoral and in the other a popliteal artery had been ligated at the time of débridement. Amputation was necessary in both cases.

In none of the wounds of the other patients in this series did cellulitis develop or was infection present grossly in the wound at the time of secondary closure. In one scalp wound and one thoracic wound, both closed at the time of the original operation, localized infections developed, which were drained.

Secondary closures were almost uniformly successful, and in the small number (estimated at 5 per cent) in which healing was not complete and drainage occurred lack of success was attributed to tension on the sutures or to the presence of dead space in the wound rather than to the presence of infection.

Mortality—Death occurred in 3 of the 645 patients injured by missiles (mortality 0.4 per cent). In 1, death was from an extensive craniocerebral wound from a 20 mm. cannon shell. The other 2 had abdominal wounds, 1 dying of fat embolism in twenty-four hours and the other of uremia from hemoglobinuric nephrosis after eighteen days. These patients are discussed more fully under the paragraphs on abdominal and craniocerebral wounds.

Return to duty was possible for 439, or 68 per cent, of the patients. Two hundred and three were sent to the United States.

ANALYSIS OF 140 CASUALTIES INJURED IN CRASHES

One hundred and forty of the 839 battle casualties (table 1) occurred as a result of crashes during combat missions. The sites of these injuries are shown in table 9. Most of the injuries were multiple.

Injuries of the head occurred most frequently. They were present in 65, or 46 per cent, of the casualties wounded in crashes. Of these, 18 had compound fractures of the skull, all with sevère injury to the brain. Eight of the fractures were depressed. Twenty-two other patients had wounds of the scalp with cerebral concussion or contusion without demonstrated fractures of the skull.

Crushing injuries to the vertebrae were the next commonest lesion. Twenty-three patients had vertebral injuries, most of which were multiple. Two had complete lesions of the spinal cord. Only 1 injury

5. Schuyler, L. H.: To be published.

6. Altemeier, W. A., and Gibbs, E. W.: Bacterial Flora of Fresh Accidental Wounds, Surg., Gynec. & Obst. **78**:164 (Feb.) 1944.

occurred in the cervical portion of the spine. All the others were in the lower six thoracic and upper four lumbar vertebrae.

Burns occurred in 14 patients. These usually involved only the face, head and neck, although 1 casualty had third degree burns over 65 per cent of his body surface.

Fifteen of the 140 patients injured in crashes died (mortality 10.7 per cent). Twelve of these died within the first twenty-four hours. All had multiple injuries and were in desperate condition when admitted. In 11 of these the immediate cause of death was thought to be an

TABLE 9.—*Site of Injury in 140 Patients Injured in Plane Crashes*

Location	Number	Injury
Head	25	Injury of scalp
	18	Injury of craniocerebral region
	22	Injury of scalp and concussion
Faciomaxillary region	4	Injury of mandible
	2	Injury of maxilla
	2	Injury of nose
Abdomen	1	Injury of gallbladder
Thoracic area	12	Injury of ribs (multiple)
Regions requiring treatment by plastic surgery	14	Burns
Soft parts	15	Contusions; sprains
Shoulder	1	Dislocation
Acromioclavicular area	2	Dislocation
Hip	4	Dislocation
Elbow	1	Dislocation
Forearm	1	Amputation
Leg	1	Leg
Fingers	2	Fingers
Long bones	1	Fracture of radius and ulna
	1	Fracture of shaft of radius
	1	Fracture of head of radius
	2	Fracture of ulna
	6	Fracture of humerus
	10	Fracture of femur
	14	Fracture of tibia and fibula
	4	Fracture of tibia
Miscellaneous sites	23	Fracture of vertebra
	6	Fracture of pelvis
	3	Fracture of clavicle
	1	Fracture of scapula
	6	Fracture of ankle
	2	Fracture of tarsal
	3	Fracture of metatarsal
	3	Fracture of carpals
	3	Fracture of metacarpal

injury of the head, while in the twelfth a crushing injury of the chest was the principal cause of death.

One patient, with a fracture dislocation of the fifth and sixth cervical vertebrae and quadriplegia, died on the third day. Another, with a compound depressed fracture of the skull through the frontal and ethmoid sinuses died of meningitis, on the eighth day. Two of the burned patients died, 1 with burns of the face, head and hands of asphyxia from edema of the larynx on the second day and the other with severe burns of 65 per cent of the body surface from toxemia and renal suppression on the fourth day. Microscopic changes of hemoglobinuric nephrosis were found in the kidneys of the last patient. The death from asphyxia was so sudden that it could not be relieved even though

a tracheotomy set was at hand and the possibility of a laryngeal obstruction had been foreseen. It could have been prevented had a prophylactic tracheotomy been done immediately on the man's admission to the hospital. This procedure was subsequently carried out on all with severe burns of the head in whom the possibility of the inhalation of flames was present.

Sixty-five, or 46 per cent, of the casualties injured in crashes were returned to duty. Sixty were returned to the United States.

ANALYSIS OF 26 CASUALTIES INJURED IN PARACHUTE JUMPS

Twenty-six men were injured in parachute jumps from disabled planes during combat missions and were hospitalized immediately. The sites of the twenty-eight injuries incurred in these 26 men are shown in table 10. All the fractures were simple ones. Sixteen men were returned to duty, and 10 were sent to the United States. None died.

TABLE 10.—*Site of Injury in 26 Patients Injured in Parachute Jumps*

Location	Number	Injuries
Long bones	2	Fracture of humerus
	2	Fracture of tibia and fibula
	4	Fracture of ankle
Miscellaneous sites	1	Fracture of pelvis
	3	Fracture of first lumbar vertebra
	1	Fracture of metatarsal
Head	3	Concussion
Faciomaxillary region	1	Maxilla
Regions requiring treatment by plastic surgery	2	Burns
Ankle	3	Sprain
Foot	1	Sprain
Back	5	Sprain

ANALYSIS OF 28 CASUALTIES RESULTING FROM PLANE ACCIDENTS

Table 1 gives an analysis of the types of accidents occurring in a plane during combat for which hospitalization was necessary. Eleven of these injuries occurred when some part of the body was caught in a moving turret. The top turret was involved in seven and the ball turret in four of these accidents. Only 3 patients were admitted for cold injury during the year of this study. This low figure is evidence of the improvement in equipment and plane design over the earlier years of the war.

Two fatalities occurred in this group. Both of the patients were tail gunners, who suffered severe injuries of the head when struck by an unexploded bomb dropped from above. Both died shortly after admission. All other patients were returned to duty except 1 in whom contusion of the radial, median and ulnar nerves from an injury by a turret necessitated return to the United States.

SUMMARY

Sixty-nine per cent of wounds from missiles received by Air Force crews in combat occur in the extremities, 11 per cent in the trunk and 20 per cent in the head and neck. Of wounds of the extremities 25 per cent result in compound fractures, 8 per cent in neural injury and 5.5 per cent in major arterial injury.

Body armor worn by the crews of heavy bombers in combat has reduced the number of penetrating thoracic and abdominal wounds.

Injuries of the head and back occurred most frequently after plane crashes and injuries of the back and ankle after parachute jumps. The commonest accident within a plane in flight is the wedging of some part of the body in a moving turret.

The bacterial flora from débrided tissues of Air Force casualties is not unlike that reported from civilian wounds occurring on the ground. The high incidence of organisms of the Clostridium group (41.2 per cent) is attributed to the presence of wool from flying suits, which was present in most of the wounds.

The low incidence of infection in wounds is attributed to the fact that adequate surgical treatment was available on an average of five and one-half hours after wounding. The use of the sulfonamide drugs and penicillin presumably contributed to the low rate of infection; however, these agents were considered to be subordinate to adequate wound débridement.

The low mortality in wounds from missiles (0.4 per cent) is attributed to skilful first aid administered in the plane and on the landing fields, to adequate surgical treatment made possible by plasma, to multiple transfusions and anesthetic administered endotracheally and to the control of infection by operation and chemotherapy. Of all these factors the use of transfusions of whole blood, which have made adequate surgical treatment possible, has contributed the most to the low mortality.

ORBICULARIS ORIS MUSCLE IN DOUBLE HARELIP

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DURING operations on 3 patients with double harelip, a modification of one of the usual plastic procedures was evolved.[1] The essential feature of this change was to join the sphincter muscles of each side across the premaxilla, and, to this end, it was necessary to cut deeply into the lip at right angles to its edge in order that a flap of sufficient length could be sewn to the corresponding structure of the opposite side. What was not known at the time was how much sphincter oris muscle was present. It is the purpose of this article to give the anatomy of this muscle in double harelip.

The structure of the orbicularis oris muscle in the lower lip is of little concern in this report. Nor is there much to say about the lip portion of the premaxilla except to record in agreement with Ritchie,[2] Veau and Plessier,[3] Boyd,[4] Peyton [5] and Mullen [6] that it has no striated muscle.

The orbicularis oris muscle is an unusual muscle not only in that its origin is in muscle but also in that some of its insertion, besides that to the skin and mucous membrane, is also in muscle. It is built around the buccinator muscle, which divides as it approaches the corner of the mouth. The middle portion of the buccinator muscle has its origin in the pterygomandibular raphe, and its fibers decussate, the superior division going along the upper portion of the lower lip and the inferior division extending along the lower portion of the upper lip. In either case the fibers meet the ones from the opposite side and, in addition, attach themselves to a less extent to the skin and least to

From the departments of anatomy and surgery of the Johns Hopkins University School of Medicine.

1. Lee, F. C.: Underlying Principles in the Repair of Double Harelip, J. M. A. Georgia **23**:383, 1934.

2. Ritchie, H. P.: Congenital Cleft Lip and Palate, Ann. Surg. **84**:211, 1926.

3. Veau, V., and Plessier, P.: Traitement du bec-de-lièvre bilatéral total, J. de chir. **40**:321, 1932.

4. Boyd, J. D.: The Classification of the Upper Lip in Mammals, J. Anat. **67**:409, 1933.

5. Peyton, W. T.: The Dimensions and Growth of the Palate in Normal Infant and in Infant with Gross Maldevelopment of the Upper Lip and Palate, Arch. Surg. **22**:704 (May) 1931.

6. Mullen, T. F.: Congenital Cleft Lip, M. J. & Rec. (supp.) **122**:402, 1925.

the mucous membrane in the general region of the midline. The uppermost fibers of the buccinator muscle, having their origin primarily in the maxilla, pass directly forward across the upper lip; the lowermost fibers, arising chiefly from the mandible, extend directly forward also across the lower lip. Superimposed on this structure there is further decussation, more superficially placed at each corner of the mouth. In this instance, the triangularis menti muscle, from below, tapers out rapidly at the corner of the mouth but extends into the upper lip. The caninus muscle, from above, projects itself downward and mingles to some extent with the triangularis muscle but in the main passes directly underneath this muscle to reach the lower lip. Both the triangularis and the caninus muscle are inserted into the skin near the midline. Immediately underneath the triangularis muscle, the platysma is inserted into the orbicularis fibers of the sphincter oris. Still superficial to the platysma at the corner of the mouth and slightly superiorly, the zygomatic and the risorius muscles also join the underlying muscle groups to form the thickening of the cheek in this general area. According to Henle, the zygomatic muscle is split into two layers at the corner of the mouth, thus forming a canal, in which the superior labial blood vessels are found. The superior and inferior incisor labialis muscles are also attached to this nodule, while the superior and inferior quadratus labii muscles are inserted more medially. Also deeply placed and still more medially are the mentalis muscle, of the lower lip, and the nasalis muscle, of the upper lip. The small muscles of Klein are short, sparse, fragmentary bundles which are situated in the lip proper, are placed at right angle to the orbicularis fibers and extend from these to the subcutaneous tissue. They are more frequent in the midline and become less in number in the lateral portions of the lips. This group of fibers is sometimes spoken of as the compressor labii.

The foregoing description of the orbicularis muscle was taken from the current anatomic textbooks, with liberal help from the older reports of Aeby [7] (1879) and Roy [8] (1890). With modern technical facilities for making serial sections and with the newer plastics for reconstructions, it may be possible to give a more complete idea of the way the different muscles contribute to the formation of the orbicularis oris muscle.

Embryologically, the sphincter oris muscle, being one of the muscles of expression whose evolution has been so well described by Ernst Huber in 1931, gradually becomes differentiated out of that mass of early muscle tissue which has its origin in the second or hyoid arch and is supplied by the facial nerve.

7. Aeby, C.: Die Muskulatur der menschlichen Mundspalte, Arch. f. mikr. Anat. **16**:651, 1879.

8. Roy, J. P.: Le muscle orbiculaire des lèvres, Thesis, Bordeau, no. 28, 1890.

The same terminology being used, the double harelip is generally described as being due to a bilateral lack of fusion between the maxillary and medial nasal processes in addition to an excessive protrusion of the premaxilla. It would seem that the lateral nasal process also did not fuse. Whether this time-honored explanation will survive is open to doubt because of recent and as yet unpublished work by Dr. George L. Streeter, Research Associate in Embryology, Carnegie Institution of Washington. His models and drawings, which I have had the privilege of seeing, give the basis for a different interpretation.

MATERIAL AND METHOD

Opportunity to study anatomically a case of double harelip was afforded by the Department of Embryology, Carnegie Institution of Washington.

The specimen, no. 5605 in the collection of the Department of Embryology, Carnegie Institution of Washington, was received on Dec. 20, 1927 from Dr. Harold Cummins, of the Department of Anatomy of the Tulane University of Louisiana College of Medicine. The marasmic Negro baby girl lived for five months. Besides the double harelip she had a cleft palate, together with partial and complete congenital amputations of the fingers of the right hand and toes of the right foot. The amputations were described by Dr. George L. Streeter [9] in a previous publication.

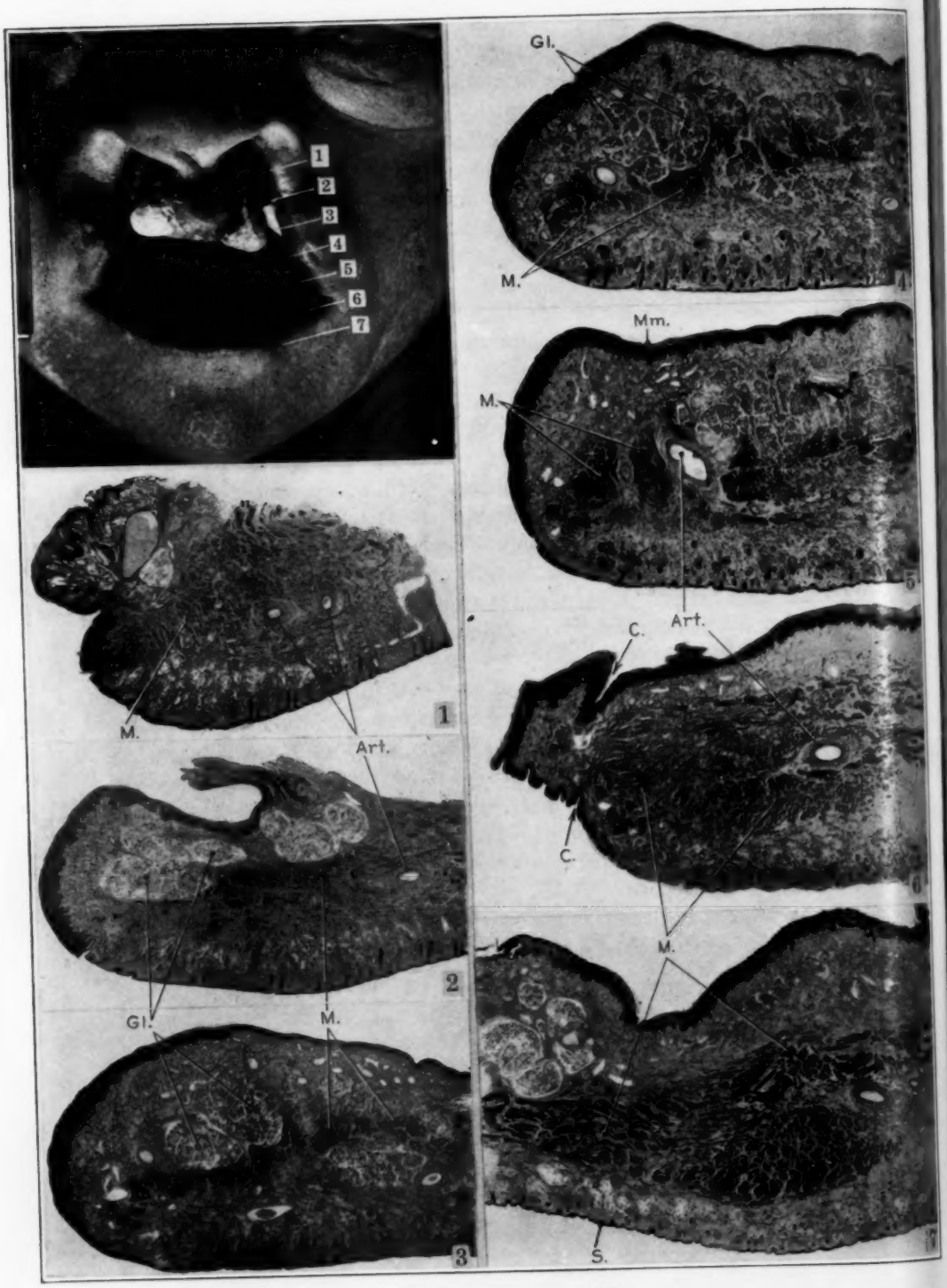
The entire body had a fixative crown to rump length of 343 mm. and was preserved in 10 per cent solution of formaldehyde.

For the study of the orbicularis oris muscle, the entire left side of the upper lip together with a portion of the left side of the lower lip was removed in one piece, embedded in colloidin and serially sectioned at a thickness of 20 microns. Every tenth section was stained in hematoxylin and eosin and mounted in balsam. This pilot series forms the basis of the report.

In addition, the right half of the labial premaxilla was taken as one block, as were individual wedges of tissue from the right side of the upper lip in order to supply sections for purposes of control.

For convenience of description, section *6* in the accompanying illustration may be considered first. This section is at the corner of the mouth and contains the largest amount of striated muscle not only relatively but also actually as far as the upper lip is concerned. The superior labial artery marks the lateral border of the cross-sectioned vertical muscle fibers which form the bulk of the orbicularis oris muscle. However, the horizontal fibers, probably the buccinator muscle, extend

9. Streeter, G. L.: Focal Deficiences in Fetal Tissues and Their Relation to Intra-Uterine Amputation, Contrib. Embryol. **22**:1, 1930.



(See legend on opposite page)

still more laterally and occupy the entire posterior portion of the muscle mass; medially they almost reach the mucocutaneous border at the corner of the mouth, where they decussate, maintaining a horizontal position as far as the lower lip is concerned (section 7) but making a sharp vertical change of direction as they enter the upper lip (section 5).

Medial to the superior labial artery is a connective tissue septum, which extends halfway to the mucocutaneous juncture. It is only about 1 mm. wide and is immediately flanked by muscle bundles, which may be portions of the split zygomatic muscle, of which the anterior portion is the larger.

Section 6 being used as a base, several contiguous cylindric bundles of muscle, all about the same size, extend upward into the central vertical plane of the lip. These columns appear gradually at successively higher levels, the first one being placed laterally and the others following in a medial direction.

The first column, beginning anteriorly and medially to the superior labial artery, continues upward and slightly laterally, being displaced by the dividing artery and finally assuming a smaller size and a posterior position. At the same time the buccal glands, which are absent in the plane of section 6, begin to appear and not only to become rapidly larger, numerous and more anterior but also to engulf and split up the column of muscle, which thins out for a short distance but then becomes thicker as it spread laterally. The muscle wall restricts in general the buccal glands to a posterior position, which they keep. However, the wall, which takes on a scalloped appearance (section 3), not infrequently allows glands to penetrate and even reach a relatively subcutaneous position (sections 3 and 4).

The second column of muscle separates out as an entity soon after the first column has appeared and continues upward directly medially to the superior labial artery, and when this vessel divides the column maintains the same relative position except that now it is lateral to the medial branch of the superior labial artery. It then breaks up in small, narrow columns, which later become thicker and more numerous, with the lateral bundles blending with the medial segments of the first column. The buccal glands do not pierce this wall of muscle.

The third column of muscle differentiates out quickly once the second column has formed. The distance between the horizontal planes

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EXPLANATION OF PLATE.

The muscle tissue in a 5 month old baby with a double harelip. Photograph of face, showing the position of the seven serial sections. *M.* indicates muscle; *Gl.*, buccal glands; *Art.*, artery; *S.*, skin; *C.*, corner of mouth, and *Mm.*, buccal membrane. The sections are magnified 8 times.

of origin of the first and third columns is about 0.8 mm. Like the second and third columns, many of the muscle fibers of the third column are derived from the buccinator muscle, of which some fibers continue horizontally anteriorly and medially to form a less distinct fourth column, which is near the mucocutaneous border of the lip.

The third column continues upward and then takes a more anterior position, being anterior and medial to the medial branch of the superior labial artery. Gradually this column becomes less compact and thinner, with its lateral segments running parallel to the contiguous medial portions of the second large column of muscle. At the same time the third column of muscle retreats a little from the medial plane but still maintains a relatively close position to the cutaneous position of the lip. Finally, the fiber bundles become only gradually more and more attentuated, until at the uppermost portion of the lip they quickly become thin, few and scattered.

The fourth column, as previously mentioned, is small, quickly turns upward, always is near the mucocutaneous junction and blends with the third column. It is about 2.4 mm. in length.

In section *2* the four columns of muscle have lost their individuality, but they still maintain a line which holds the buccal glands in a posterior position. The increased frequency of longitudinally cut fibers suggests the influence of the quadratus labii superioris muscle. The dearth of muscle near the mucocutaneous border indicates a lateral displacement of the muscle columns.

In section *1* the muscle columns have entirely disappeared, and the muscle tissue is in numerous, widely dispersed small muscle bundles situated relatively deep to the skin. Buccal glands are scant, and hyaline cartilage appears.

Below the corner of the mouth, it will be seen from section *7* that the mass of muscle is primarily the buccinator and caninus muscles situated posteriorly, with the triangularis muscle predominating anteriorly. Buccal glands are also present.

COMMENT

In presenting actual photographs of sections taken through the lip of a person who had a double harelip, a more accurate record is available than if a composite drawing had been made.

To what extent normal structures, like the buccinator muscle, contribute to the formation of the orbicularis muscle in an abnormal condition like a double harelip can only be conjectured. Accordingly, no claim is made for the accuracy in the explanation of the participation of specific muscles.

Study of the serial sections of the corner of the mouth of this 5 month old specimen casts some doubt on the structure of the adult

orbicularis oris muscle as pictured in the anatomic textbooks. These books show a heavy development of concentric sphincter muscles at the angle of the mouth. The specimen of this report showed almost the exact opposite, namely, relatively few sphincter muscle bundles but a heavy mass of horizontal fibers which extend close to the free border of the lip.

The buccal glands in volume may occupy as much as a quarter of the entire lip in the upper sections. In the lower sections, near the corner of the mouth, many of the glands are partly surrounded by muscle columns, which, through their contractions, might add appreciably to the emptying mechanism of the glands.

The loose distribution of the muscle bundles, together with the absence of well developed perimysial membranes, recalls the anatomic basis for the rapid spread of an acute infection of the upper lip.

SUMMARY

In order to study the orbicularis oris muscle, serial sections were made of the left side of the upper lip of a 5 month old human specimen having double harelip.

It was found that this muscle is well developed at the corner of the mouth but quickly becomes thin and fragmented as the ala of the nose is reached. It is moderately effective in forming a barrier to keep the buccal glands in a posterior position in the lip.

No support was found for the view that there is a large concentration of purely sphincter muscle fibers at the corner of the mouth.

The Department of Embryology, Carnegie Institution of Washington, and its director, Dr. George W. Corner Sr., as well as his predecessor, Dr. George L. Streeter, contributed the material on which this report is based.

FATALITIES FOLLOWING WAR WOUNDS OF THE ABDOMEN

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SINCE the ending of World War II many papers have been published dealing with abdominal injuries in warfare. Emphasis has been placed on patients that survived operation. This paper is presented as an analysis of the extent of injury and the cause of death of those who did not survive intra-abdominal injuries.

This material was obtained from records of an active evacuation hospital and from two surgical teams working with active field hospitals. All autopsies in cases of death in the evacuation hospital were done by a pathologist attached to the unit. In the field hospitals, autopsies were done by an operating surgeon and were therefore limited because of the heavy burden thrust on the surgical teams.

In this series of patients there were 91 deaths following major abdominal wounds, and in 75 per cent of this group autopsies were performed. All patients had suffered major visceral and/or vascular damage. All thoracoabdominal injuries have been excluded. It will be noted that many of the patients in this series had other major associated wounds, such as compound fractures, injuries of the head and traumatic amputations.

Four hundred and forty-three patients with intra-abdominal wounds were operated on by us or under our direction. There was an operative mortality of 16.7 per cent. Two hundred and eighty-four patients with penetrating wounds of the abdomen were admitted to the evacuation hospital. Seventeen, or 5.6 per cent, died without operation. Of 877 patients with penetrating wounds of the abdomen admitted to the field hospital where many of these operations were performed, 57, or 6.49 per cent, died before operation could be undertaken. We feel that the latter figures are more important than the operative mortality. The low preoperative mortality indicates that little selectivity was exercised and that a high percentage of seriously wounded patients were given the small chance that operation could offer. Many of these patients were moribund on admission, usually as a result of overwhelming hemorrhage or severe peritonitis. Others were admitted with wounds incompatible with life despite operation. A few died while waiting for operation, as a result of a large preoperative reserve,

which on occasions was as high as 400 patients. It is probable that a few in the latter group might have been saved if operation could have been undertaken earlier. It will be noted later in the paper that many patients were sent to the operating room although it was doubtful that they would survive the operation. The deaths following the induction of anesthesia were listed as postoperative deaths.

Sixty-three of this series of nonsurvivors were American soldiers, 20 were prisoners of war and 8 were allied or enemy civilians. The percentage of bullet wounds (38 per cent) is higher in this series than that stated by Cutler [1] for war wounds in general (29 per cent) seen in the First United States Army. Imes [2] reported bullet wounds in 22 per cent of his series of penetrating wounds of the abdomen. Shell fragments (artillery, mortar, bomb and grenade) caused 58 per cent of the wounds, and 4 per cent remained unclassified in this series.

SHOCK

Sixty-five of the 91 patients who died were admitted in profound shock. Almost half (30 patients) responded poorly or not at all to the usual treatment with whole blood, plasma, arrest of visible hemorrhage and splinting of fractures. The cause of the shock could not be ascribed to any one factor except in occasional instances but, for the most part, was a combination of hemorrhage, evisceration of abdominal contents, severe intraperitoneal contamination and what Hardt and Seed,[3] and Jolly [4] referred to as the "retroperitoneal syndrome."

Hemorrhage was the outstanding feature of nearly one third (20 patients) of the patients admitted in severe shock. The diagnosis of shock due to hemorrhage in patients with multiple severe concomitant injuries was not difficult. The additional diagnosis of severe intra-abdominal hemorrhage in such patients frequently presented a difficult problem. Failure to respond to the liberal use of whole blood within two hours was usually considered sufficient evidence to suspect intra-abdominal hemorrhage. Patients thus suspected frequently were found at operation to have peritoneal cavities full of blood but with no active bleeding present. The manipulation of exploration or repair of intraperitoneal injuries usually dislodged clots which revealed the location of an injury to a major vessel.

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1. Cutler, E. C.: Military Surgery, United States Army, European Theater of Operation, 1944-1945, Surg., Gynec. & Obst. **82**:261, 1946.

2. Imes, P. R.: War Surgery of the Abdomen, Surg., Gynec. & Obst. **81**:608, 1945.

3. Hardt, H. G., Jr., and Seed, L.: Thoracoabdominal Gunshot Wounds, Arch. Surg. **46**:59 (Jan.) 1943.

4. Jolly, D. W.: Field Surgery in Total War, New York, Paul B. Hoeber, Inc., 1941.

Eighteen (19.8 per cent) patients had abdominal viscera protruding from the peritoneal cavity. The accompanying contamination, drag on the mesentery and impairment of blood supply to the viscera involved were factors which made this complication respond poorly if at all to supportive therapy, even in the absence of accompanying severe hemorrhage. The high mortality (63.8 per cent) of this serious complication is pointed out by Bradford and colleagues.[5]

The most consistent contributing factor to shock was severe fecal contamination of the peritoneal cavity, occurring in about 70 per cent of the cases. Patients with severe peritoneal contamination alone frequently survived, with remarkably smooth convalescence. Accompanied with multiple severe injuries, severe hemorrhage or extensive retroperitoneal damage, it often provided sufficient additional insult to produce a fatality.

Jolly [4] has described a syndrome of retroperitoneal injury accompanied with severe shock in the absence of excessive bleeding or peritoneal contamination. He stated the belief that the shock is of neurogenic origin. Two of our patients may possibly fall into this group. Both, however, had severe fecal contamination of the retroperitoneal tissues.

REPORT OF CASES

CASE 1.—An American soldier sustained a gunshot wound (machine gun) of the right side of the lower part of the abdomen. On admission eleven hours later, his pulse was imperceptible and his blood pressure was below 80 systolic. Administration of 1,500 cc. of blood and 500 cc. of plasma produced no significant improvement during the next six hours, and with the patient under anesthesia by bilateral intercostal block celiotomy was undertaken.

There was no significant intraperitoneal fecal soiling, but the retroperitoneal portion of the cecum was severely lacerated and there was an extensive laceration of the retroperitoneal tissues. The kidney was undamaged, but there was a small compound fracture of the right wing of the ilium at the site of the wound of exit. A cecostomy was carried out and the retroperitoneal tissues débrided and drained. The patient withstood the procedure well but remained in shock and succumbed twelve hours following operation. Clinically, the case was not considered a case of renal failure.

CASE 2.—An American soldier sustained a gunshot wound (rifle) of the right side of the lower part of the abdomen. He was admitted within three and one-half hours, in severe shock. During the preoperative administration of 1,000 cc. of blood and 250 cc. of plasma his blood pressure continued to fall, and intra-abdominal hemorrhage was suspected. Two and one-half hours after admission, he succumbed during the operative procedure. Autopsy revealed only minimal hemorrhage and no injury except a lacerated cecum with severe retroperitoneal damage and considerable fecal contamination to the retroperitoneal tissues. There was no gross or microscopic evidence of renal damage.

5. Bradford, B., Jr.; Battle, L. H., and Pasachoff, S. S.: Abdominal Surgery in an Evacuation Hospital, Ann. Surg. **123**:32, 1946.

It can be seen in table 1 that 16, or 17 per cent, of the patients had major vascular injuries within the abdomen. All were associated with visceral injuries except in 3 instances. Twenty-eight per cent had three or more intra-abdominal organs injured. Seventy-eight per cent had two or more organs injured. Twenty-two per cent had only

TABLE 1.—*Tabulation of Abdominal Organs Injured*

Organs Injured	No. of Cases
Colon, small intestine	20
Small intestine	11
Colon, small intestine, bladder	8
Colon	7
Colon, great vessel	6
Colon, kidney	5
Small intestine, bladder	3
Colon, small intestine, great vessel	3
Great vessel	3
Kidney	3
Colon, bladder	2
Colon, liver	2
Colon, small intestine, liver	2
Small intestine, great vessel	2
Stomach	2
Liver, kidney	2
Colon, small intestine, stomach	1
Colon, small intestine, liver, kidney	1
Colon, small intestine, liver, bladder	1
Small intestine, kidney	1
Small intestine, great vessel, bladder	1
Stomach, liver	1
Stomach, liver, kidney, pancreas	1
Liver	1
Liver, kidney, great vessel	1
Blast (subserosal hemorrhage of the colon and small intestine).	1

one organ injured. It is important to note that 72 per cent of this series had other major associated lesions, such as compound fractures, injuries of the head or extensive wounds of the soft tissues. For these patients, who survived transport to the nearest hospital, this

TABLE 2.—*Associated Major Injuries*

Injuries	No. of Cases
Compound fracture of long bones	36
Extensive damage to the muscles (buttock, thigh)	27
Compound fracture of pelvis	20
Multiple severe lacerations	16
Compound fracture of vertebrae	11
Penetrating wound of brain	5
Major vessel lacerated or divided, with impairment of blood supply to an extremity	5
Traumatic amputation of an extremity	4
Trench foot, severe	1

factor of multiplicity of severe injuries was responsible for far more deaths than the severe damage of one vital organ. An analysis of major injuries other than intra-abdominal is shown in table 2.

CASE 3.—An American soldier sustained wounds by high explosive shell fragments. He was admitted eleven hours later, at which time his blood pressure was unobtainable and pulse imperceptible. He was pale and had constant

nausea. Administration of 500 cc. of blood in 500 cc. of Alsever's solution[6] was begun immediately, but soon afterward the patient had a violent reaction to the transfusion. One thousand cubic centimeters of plasm was given. Following its administration, his blood pressure rose to 104 systolic and 78 diastolic and his pulse rate to 120. In the meantime clinical and roentgenologic examination revealed the following wounds:

1. Penetrating wound of the abdomen
2. Compound fracture of the left femur
3. Compound fracture of the left tibia and fibula
4. Compound fracture of the right radius and ulna
5. Compound fracture of the right scapula
6. Severe lacerations of the left thigh and lower part of the leg
7. Penetrating wounds of the right thigh, scrotum, penis and neck
8. Foreign bodies (by roentgenologic examination) in neck, right upper quadrant of abdomen, pelvis and at site of all compound fractures

Operation was carried out ten hours after admission, at which time the patient had twelve perforations of the small intestine closed. All wounds were débrided and appropriate plaster encasements applied. The patient had 500 cc. of blood and 500 cc. of plasma during operation. He remained anuric during his postoperative period and succumbed fifty-four hours after operation. Autopsy revealed the following additional significant findings: (1) pulmonary infarction in the lower lobe of the right lung, (2) hemoglobinuric nephrosis and (3) moderate peritonitis. We believe that this patient received too little blood. The cause of death was undoubtedly due to renal ischemia on the basis of (*a*) prolonged inadequately treated shock and (*b*) violent reactions to transfusions.

SURGICAL PROCEDURE

Thirteen (17.5 per cent) of the patients on whom some major surgical procedure was carried out died during operation. A few of these severely injured patients died during the induction of anesthesia, but the deaths were considered operative deaths. Later in the campaign, anesthesia by bilateral intercostal block was used rather than the inhalation type on the patients who presented bad risks. This substantially reduced the operative mortality in this type of patient, though it may have had little effect on the ultimate outcome in the case. On the 75 patients operated on the following procedures were done:

	No. of Patients
Exteriorization of wounded large bowel	40
Resection of small intestines, with anastomosis	27
Repair of lacerations of small intestine	27
Débridement and immobilization of compound fractures of long bones	25
Suprapubic cystotomy and repair of bladder	11
Ligation of great vessel	9
Liver packed	5
Repair of the colon (distal to colostomy)	4
Nephrectomy	4
Amputation	4
Liver sutured	3
Kidney sutured	3
Repair of stomach	3
Craniotomy	2
Resection of colon	2
Repair of ureter	1
Repair of great vessel	1
Incision and drainage of intraperitoneal abscess	1

6. Alsever's solution contains 0.80 per cent sodium citrate, 2.05 per cent dextrose and 0.42 per cent saline solution in an isotonic solution of sodium chloride.

Loria [7] has emphasized the importance of the operating time. In his series of cases the mortality was considerably higher when the operating time exceeded one and one-half hours. The length of time a patient is subjected to anesthesia and the trauma of operation are of considerable importance. The difference in mortality in our experience was not due to length of the operation but to the severity and number of the injuries.

PREOPERATIVE DEATHS

Sixteen patients died without benefit of operation. Several factors were responsible for this. The condition of the patient and seriousness of the injury, the rapidity with which death followed the patient's admission to the shock ward and our inability to operate on every patient at the optimum time, due to a reserve of seriously injured patients, are the most important factors. For example, 50 per cent died within four hours after being admitted to the shock ward and one-half of this number within one hour. Obviously, most of these patients would have succumbed had operation been undertaken during this period.

The problem of how much shock therapy these moribund patients should receive, especially in relation to the number of hours following injury or admission, and the availability of operating room space and personnel become, at times, extremely complex. It is the natural inclination of every surgeon or triage officer in choosing between 2 seriously injured patients for operation to choose the one who has made a satisfactory response to shock therapy and to allow the pulseless, pressureless patient to receive more blood, with the hope that his response may be a delayed one. If this patient then succumbs after four or five or more hours in the shock ward, some criticism may be leveled at persons responsible for allowing him to remain unoperated on for so long. Most surgeons, in our experience, made a constant and conscientious effort to operate on all the patients presenting bad risks as soon as possible. The patients not responding to shock therapy for suspected hemorrhage were given the highest priority, regardless of risk.

A few patients suffered more than the usual delay in being returned to the hospital, because of the tactical situation and as a result often were more completely exsanguinated than their more fortunate companions. This seemed especially true in cases of prisoners of war who obviously had to be overrun and captured before being returned to a hospital for medical attention. An additional factor was the apparent policy of the enemy to leave behind the severely wounded persons on evacuation of a position. These factors account, to some

7. Loria, F. A.: Penetrating Gunshot Wounds of Abdomen, South. M. J. **36**:87, 1943.

extent, for the high percentage of prisoners of war (43 per cent) in this group in which no operation was performed.

A more detailed analysis of this group of patients may be found in table 3.

CAUSE OF DEATH

Insofar as possible an attempt was made, either at clinical examination or at autopsy, to determine the cause of death. In classification of the cases, considerable overlapping of contributing factors was present. The patients who died as a direct result of hemorrhage presented no particular problem.

A great number of patients, however, without an excessive amount of hemorrhage were admitted in a state of shock and died shortly after operation, apparently as a result of shock. They may or may not have responded satisfactorily to the usual supportive measures. All of them had severe, widespread, intraperitoneal fecal contamination, which, in our opinion, was the chief factor in contributing to their death. Such patients have been listed in table 4 under "shock and acute peritonitis." This is not to imply that all such patients succumbed, for persons with experience in either World War I or World War II can undoubtedly recall many similar patients who made remarkably smooth recoveries.

Patients who failed to survive because of widespread peritonitis are classified in table 4 under "peritonitis." These, for the most part, were patients with severe peritonitis who survived for a few days and then succumbed. Their pathologic process was purely one of infection, and the entire clinical and pathologic picture unassociated with shock. Frequently these patients had continuous sources of contamination, such as an overlooked hollow visceral perforation or a suture line that had failed to hold.

Two cases were classified under "retroperitoneal syndrome," previously discussed.

Hemolytic reactions to transfusions were thought to be responsible for death in 6 cases, and in 4 cases microscopic sections of the kidney were diagnosed as hemoglobinuric nephrosis. The reports on the other 2 cases were never received from the laboratory, but from the clinical and gross pathologic findings they fell into the same group.

Seven patients were believed to have died from pulmonary complications. All were reported to have had pneumonia. In addition, 3 had evidence of lobular infarction, but no patient was found to have died from a massive pulmonary embolus.

Associated major injuries were responsible for 5 cases of death, in 3 of which the patients never reached operation. These included cases of a severely damaged brain, an infected compound fracture of

TABLE 3.—*An Analysis of Cases in Which Operation Was Not Performed*

Nationality and/or Status of Patients	Interval Between Injury and Admission, Hr.	Interval Between Admission and Death, Hr.	Extent of Abdominal Injury	Significant Associated Major Injuries	Cause of Death, Based on Autopsy Findings	Comments
German civilian	?	20	Severe laceration of pelvic colon	Severe lacerations of buttocks; compound comminuted fracture of vertebrae	Peritonitis	Obvious severe peritonitis on admission
French civilian	?	4	?	Penetrating wounds of buttocks, arm and scrotum	No autopsy	On admission thought to have intra-abdominal hemorrhage
American	1	14	Laceration of vena cava	None	Hemorrhage	
Prisoner of war	?	48	Laceration of superior mesenteric vessels	None	Hemorrhage	
Prisoner of war	?	20	Laceration of common iliac vein; penetrating wound of rectum	Compound comminuted fractures of ilium and hand	Hemorrhage	
Prisoner of war	12	½	Laceration of iliocolic artery; perforating wound of cecum and ileum	Compound comminuted fractures of ilium and hand	Hemorrhage	
Prisoner of war	?	43	Penetrating wound of cecum, sigmoid and ileum	Compound comminuted fractures of sacrum, ilium, femur, radius and ulna	Severe peritonitis	Blood pressure never above 60 systolic
American	4	25	Evisceration of ileum and transverse colon; perforating wounds of colon, jejunum and ileum	None	Severe peritonitis	Blood pressure and pulse always unobtainable; comatose
American	?	1	Perforating wound of cecum and ascending colon	Severe penetrating wound of brain	Severe damage to brain	
American	2 days	6½ days	One perforation of ileum	Infected compound comminuted fracture of femur	Severe infection; compound fracture of femur; no peritonitis	Incision and drainage of the thigh; hip spica; observation on abdomen
Prisoner of war	?	3	Transection of sigmoid, colon and ileum	Compound comminuted fracture of ilium; penetrating wound of buttocks	Severe peritonitis	No tourniquet in place on admission
American	5	1/12	Perforating wound of stomach	Compound comminuted fracture of tibia and fibula; severed anterior and posterior tibial arteries and radial and ulnar arteries	Hemorrhage	
Prisoner of war	?	¼	Perforated ileum and colon; lacerated mesenteric vessels	Compound comminuted fracture of ilium	Hemorrhage	
Prisoner of war	?	3	Severe laceration of kidney	Compound comminuted fracture of vertebra	Hemorrhage	
American	4 days	24	Perforating wound of ileum, colon and bladder	Compound comminuted fracture of femur, radius and ulna and pelvis	Severe peritonitis	

the femur and an exsanguination from lacerated vessels of the extremities. A severely damaged brain and gas gangrene of the buttocks accounted for the 2 deaths from associated injuries in the group in which operation was performed.

Eight cases were listed as "unclassified." Included in this category were 1 case of death from the anesthetic (pentothal sodium); 1 case in which the patient was reported to have died from aspiration of a large quantity of vomitus; 1 case of death from blast; 1 case in which sudden death occurred following removal, on the seventh postoperative day, of a large hepatic pack and in which autopsy revealed no explanation for the death; 1 case in which death followed dehiscence of a wound and abdominal evisceration on the eighth postoperative day, and 3 cases in which no cause of death could be determined.

TABLE 4.—*Cause of Death*

Cause	Total Cases	Operated On	Not Operated On
Shock and hemorrhage	21	13	8
Shock and acute peritonitis	19	19	0
Peritonitis	23	18	5
Hemolytic reaction to transfusion	6	6	0
Retroperitoneal syndrome	2	2	0
Pulmonary complications	7	7	0
Associated major injuries	5	2	3
Unclassified	8	8	0
	91	75	16

ERRORS OF SURGICAL JUDGMENT

It is inevitable that some errors will be committed in the management of nearly 450 patients with penetrating wounds of the abdomen. Many were patients for whom treatment was difficult and in whom a certain percentage of error may have been excusable. Others were committed under the burden of an extremely heavy load of patients or other trying conditions. Obvious errors in this series of patients who died fall into the following groups:

	No. of Patients
Unrecognized penetrating wounds of the abdomen	2
Overlooked perforations of hollow viscera	6
Improper use of pentothal sodium	1
Failure to apply a tourniquet	1

Many patients conceivably could have been called mishandled, because they were taken to the operating room before or after the optimum time for operation. The amount of shock therapy a patient should receive is a relative matter and depends largely on the tentative diagnosis. Patients with suspected hemorrhage not responding to shock therapy were operated on much sooner than those without the probability of severe hemorrhage.

Two patients had unrecognized penetrating wounds of the abdomen. Neither had wounds penetrating the abdominal wall, the wound of entry having been in the thigh in both patients.

CASE 4.—An American soldier was admitted forty-eight hours after injury. His only wound was a severe compound comminuted fracture of the middle and lower third of the left femur. The muscles of the thigh were badly damaged. At the time of admission, frank pus was present in the wound and the soft tissues were edematous and friable. Roentgenologic examination accidentally revealed a small shell fragment in his pelvis, probably within the peritoneal cavity. His condition was poor, but there was no clinical evidence of peritonitis or intra-abdominal bleeding. Incison and drainage of the thigh, with application of a plaster encasement, was carried out. Celiotomy was considered but decided against because of the extremely poor condition of the patient. His course was continually downhill, and he died three days later.

Autopsy showed a single perforation of the ileum, which had effectively sealed itself off and was surrounded only by a small area of localized peritonitis. Death was attributed to sepsis as a result of extensive infection of the thigh.

CASE 5.—An American soldier was received as a transfer from a field hospital on his third postoperative day. He previously had had débridements of compound fractures of the femur and radius. Roentgenologic examination also revealed a fractured pelvis. From the record, celiotomy had not been considered. At the time of admission, his condition was extremely poor and he had evidence of generalized peritonitis. He died twenty-four hours after admission.

Autopsy revealed severe generalized peritonitis with multiple perforations of the ileum, sigmoid colon and urinary bladder.

One of the dangers of a "too hurried" operation is an overlooked perforation of a hollow viscus. Severe intraperitoneal hemorrhage and extensive concomitant injuries necessitate a lengthy operative procedure. A tendency to "speed through" a seemingly untouched corner of the abdomen is usually responsible for such errors. Hamilton and Duncan [8] in discussing overlooked perforations, reported an incidence of 30 per cent in 30 autopsies. Other authors report somewhat higher figures:

	Percentage	No. of Autopsies
Oberhelman and LeCount [9]	55.5	169
McGowan [10]	55.5	27
Taylor [11]	43	14
Billings and Walking [12]	19	49
Rippy [13]	50	12
Wilson [14]	50	20

8. Hamilton, J. E., and Duncan E:. Penetrating Gunshot and Stab Wounds of the Abdomen, Surgery **13**:107, 1943.

9. Oberhelman, H. A., and LeCount, E. R.: Peacetime Bullet Wounds of the Abdomen, Arch. Surg. **32**:373, 1936.

10. McGowan, F. J.: Penetrating Wounds of the Abdomen, Ann. Surg. **102**:395, 1935.

11. Taylor, F. W.: Gunshot Wounds of the Abdomen, J. Indiana M. A. **31**:342, 1938.

12. Billings, A. E., and Walking, A.: Penetrating Wounds of the Abdomen, Ann. Surg. **94**:1018, 1931.

13. Rippy, E.: The Management of Perforating Gunshot Wounds of the Abdomen, South. Surgeon **10**:441, 1941.

14. Wilson, F. C.: Gunshot Wounds of the Abdomen, South. M. J. **27**:805, 1934.

When cases in which operation was not performed and those in which death occurred during operation are excluded, in 6 of 38 cases which came to autopsy in our series perforations of a hollow viscus were found to have been overlooked, an incidence of 15.8 per cent.

The 1 death attributed to anesthesia was considered to be an error. In a soldier having a severe wound of the abdomen with evisceration but with only moderate shock, 0.25 Gm. of pentothal sodium was used for induction of anesthesia. The patient quickly succumbed, and all efforts to resuscitate him failed.

One patient became exsanguinated from hemorrhage of lacerated vessels of the extremities. He was admitted without a tourniquet in place, and from his record no tourniquet had been applied. The instruction so frequently given to medical officers and their corpsmen in the forward areas concerning the unwarranted sacrifice of limb as a result of application of tourniquets may have allowed some to become overcautious in their use, and this may possibly be considered an example.

SUMMARY

1. An analysis of 91 cases of death from intra-abdominal injury seen in evacuation and field hospitals of the First United States Army is presented. Seventy-five per cent of the cases came to autopsy.

2. Approximately 5 per cent of patients dying after receiving abdominal wounds died without operation having been undertaken.

3. Nineteen and eight-tenths per cent of the patients who died had evisceration of abdominal contents on admission to the hospital. Nearly three fourths of the patients had concomitant major injuries.

4. Seventeen and one-half per cent of this group died during operation.

5. The causes of death and errors in surgical judgment are discussed.

PRODUCTION OF EXPERIMENTAL PORTAL HYPERTENSION IN THE DOG

Anatomy of the Hepatic Veins in the Dog

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VENOUS congestion of the liver by constriction of the posterior vena cava anterior to the kidneys has been produced by others.[1] Death generally follows five to ten hours after the complete ligation of the cava just above the renal veins.[2] If the animal survives, such a procedure results in congestion not only of the hepatic and portal systems but also of the systemic regions drained by the cava caudad to the obstruction, particularly the kidney. The present work was undertaken with the object of producing hepatic congestion and accompanying portal hypertension in the dog, without the associated congestion of the systemic system.

When the experiments were undertaken, a number of difficulties in the attainment of this objective became apparent. These arose from the fact that in the dog no satisfactory description of the anatomic relationships of the hepatic veins and of their relation to the posterior vena cava was available in the published literature. A special study of these relationships was, therefore, carried out.

Forty-six livers were used in the anatomic studies. Five hardened livers were dissected in which the vena cava had been injected with a colored gelatin mass. In addition, one corrosion preparation was made, in which the posterior vena cava and the hepatic veins, down to the small tributaries, had been filled with a solution of Vinylite in

This work was carried out in the departments of Experimental Surgery and Anatomy, New York University College of Medicine, and was aided by a grant from the Dazian Foundation for Medical Research.

1. (*a*) Montemartini, G.: Contributo sperimentale all chirurgia della vena cava inferiore, Policlinico (sez. chir.) **41**:593 (Nov.) 1934. (*b*) Rohde, G.: Die Stauung der unteren Hohlvene von dem rechten Herzen und ihre Bedeutung im Krankheitsbilde der Pericarditis adhaesiva, Deutsche Ztschr. f. Chir. **203-204**:18 (May) 1927. (*c*) Zimmerman, H. M., and Hillsman, J. A.: Chronic Passive Congestion of the Liver, Arch. Path. **9**:1154 (June) 1930.

2. Whittenberger, J. L., and Huggins, C.: Ligation of the Inferior Vena Cava, Arch. Surg. **41**:1334 (Dec.) 1940. Montemartini.[1a]

acetone. Forty freshly removed livers were dissected without any special preparation. While the number of livers is admittedly not large, the surprising fact emerged that little variation was encountered in the cases studied. The accompanying diagram (fig. 1), with the exception of the slight variation noted in the following material in the drainage of the papillary lobe, might have been made directly from any one of the livers.

In the following description the terms of position employed are those in common use in comparative anatomy, "dorsal" and "ventral" being

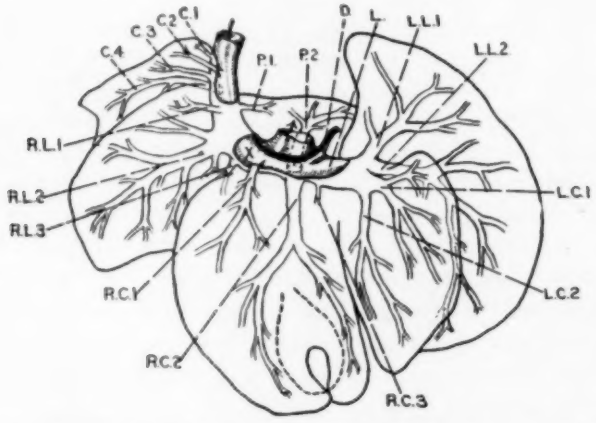

Fig. 1.—Diagrammatic anterior view of the dog's liver, represented as a transparent object, to show the pattern of the hepatic veins. The liver has been spread somewhat, to obtain a view of its entire parietal outline. Unshaded veins are within the hepatic substance. The shaded portions represent venous surfaces not in contact with liver. The solid black band crosses the vena cava where that vessel pierces the diaphragm. The arrows indicate the direction of blood flow through the vena cava. The broken line indicates the outline of the gallbladder. *C.* indicates the caudate lobe, *P.* the papillary lobe, *R. L.* the right lateral lobe, *R. C.* the right central lobe, *L. C.* the left central lobe and *L. L.* the left lateral lobe. Further explanation is in the text.

synonymous with the "posterior" and "anterior" of gross human anatomic terminology and "anterior" and "posterior" with the "superior" and "inferior" respectively of the latter.

The posterior vena cava is lodged in a deep groove on the dorsal aspect of the right lobe. In all the livers examined, this groove was converted into a tunnel for about the last half inch (1.2 cm.) just posterior to the diaphragm, by the presence of a thin bridge of hepatic tissue passing dorsal to the vena cava, between the right lateral and papillary lobes (fig. 1). From the superoventral surface of the right central lobe the peritoneum is reflected not directly onto the diaphragm but first onto the vena cava, so that this portion of the vein may be seen through the peritoneum in the living animal if the liver is depressed and the diaphragm raised (marked *X* in figure 1).

The course of the posterior vena cava, where the vein is in contact with the liver and hence capable of receiving hepatic veins, may be conveniently divided into three parts. Of these, the first is intimately related to the caudate lobe; the second is the portion previously noted as being entirely surrounded by hepatic substance and hence is related to the right lateral and papillary lobes, and the third part immediately precedes the passage of the vein through the diaphragm. It is intimately related to the right central and papillary lobes and includes the portion of the vessel previously noted as being visible through the peritoneum, between the liver and the diaphragm.

In the first part of its course the vena cava receives four veins, of somewhat variable size, which enter its lateral aspect and constitute the entire drainage of the caudate lobe (*C1 to C4,* fig. 1). In the second part of its course the vena cava receives laterally three veins from the right lateral lobe and medially one from the papillary lobe. Of the three veins draining the right lateral lobe, the second is by far the largest, conveying most of the blood from that lobe. The vein from the papillary lobe is of variable size and in no case constitutes the entire drainage of that lobe. In the last part of its course, before piercing the diaphragm, the vena cava receives two veins from the right central lobe; of these, the second is the larger (*R.C. 2,* fig. 1) and drains the entire area of the gallbladder. It also receives a vein from the papillary lobe (*P.2*) and a large vein, which is here called the left hepatic vein (*L,* fig. 1).

The drainage of the papillary lobe constitutes the only variable of importance seen in the study. In 1 case the entire drainage of this lobe was into the third part of the vena cava. In all others the drainage was partly into the second part (*P.1*) and partly into the third (*P.2*). In 1 case these two hepatic veins were of approximately equal size, while in the remainder the vein joining the third part of the vena cava (*P.2*) was the larger.

The left hepatic vein joins the vena cava almost at right angles to the course of the latter. At its termination it is not entirely enclosed by liver but, like the cava itself, is covered anteriorly only by peritoneum and may be clearly seen in the living condition through the peritoneum, where that membrane is reflected from the diaphragm onto the anteroventral surface of the liver. The left hepatic vein constitutes the entire drainage of the left lateral and left central lobes. It is formed within the liver, at the base of the cleft separating these two lobes, by the junction of a large vein from each. Each of these veins is, in turn, a short trunk formed by the junction of two veins from its own lobe (*L.L.1* and *L.L.2* and *L.C.1* and *L.C.2,* fig. 1). Just before it enters the vena cava the left hepatic vein receives a small tributary from the medial margin of the right central lobe (*R.C.3*). At its point of junction with

the vena cava, the left hepatic vein further receives a vein of considerable size, which emerges from the substance of the diaphragm (*D*, fig. 1).

On the basis of these anatomic findings, no practical experimental approach on the hepatic veins directly suggested itself. In some early experiments, Winternitz [3] ligated the hepatic veins in the dog and found no changes in the liver. In 1925 Simonds and Brandes [4] reported a method of producing experimental portal hypertension in the dog by occluding the hepatic veins without interfering with the blood flow through the posterior vena cava. Briefly, their method consisted in passing one end of a rubber tube (Rehfuss stomach tube) along the right side of the falciform ligament, between the liver and the diaphragm, through the membranous portion of the triangular ligament, thence through the epiploic foramen, up through the membranous portion of the left triangular ligament and along the left side of the falciform ligament, between the liver and the diaphragm. In this way, when the two ends of the tube were approximated, all the hepatic lobes were included within the loop. By exerting traction anteriorly and caudad on the ends of the rubber tube and at the same time producing counterpressure on the hepatic substance between the limbs of the tube, they claimed that it was possible to constrict the hepatic veins as they enter the posterior vena cava without lifting the liver out of its bed and so to avoid constriction of the vena cava. They offered as proof of this contention the observations that there is no distention of the femoral veins and that peptones, when injected into the femoral veins of experimental animals, produced systemic effects as rapidly as in control animals.

More recently, Armstrong and Richards [5] carried out similar experiments, but with some modification. They passed an occlusive ligature through the foramen of Winslow, forward over the left dome of the liver, around the anterior edge of the falciform ligament and backward over the right dome of the liver. To reduce the occluded tissue to a minimum the triagular ligaments were divided. The tie was made at the foramen of Winslow, and the ligature was left in place. Only 3 of the 9 dogs operated on survived. The remaining 6 died from hemorrhage caused by an inadvertent tear of the liver, from simultaneous occlusion of the posterior vena cava or from complete rapid occlusion of only the hepatic veins.

Several attempts were made to produce venous congestion of the liver by the method of Simonds and Brandes in the experiments herein described. None of the 46 dogs examined had a falciform ligament.

3. Winternitz, M. C.: The Effect of Occlusion of the Various Hepatic Veins upon the Liver, Bull. Johns Hopkins Hosp. **22**:396 (Nov.) 1911.

4. Simonds, J. P., and Brandes, W. C.: The Effect of Obstruction of the Hepatic Veins on the Systemic Circulation, Am. J. Physiol. **72**:320 (April) 1925.

5. Armstrong, C. D., and Richards, V.: Results of Long Term Experimental Constriction of the Hepatic Veins in Dogs, Arch. Surg. **48**:472 (June) 1944.

In about half the dogs there was a fragile, fibrous cord extending from the umbilicus to the portal fissure; this probably was an obliterated umbilical vein. In addition, when the operation was carried out a kinking of the posterior vena cava always occurred, presumably due to the fact that for part of its course the cava is completely surrounded by hepatic tissue. In these experiments there was little distention of the femoral veins, although the vena cava was completely occluded at the base of the liver. This lack of distention appears to be related to the existence in the dog of collateral venous pathways which are capable of returning the blood to the heart with little or no delay (see figure 2 *B*).

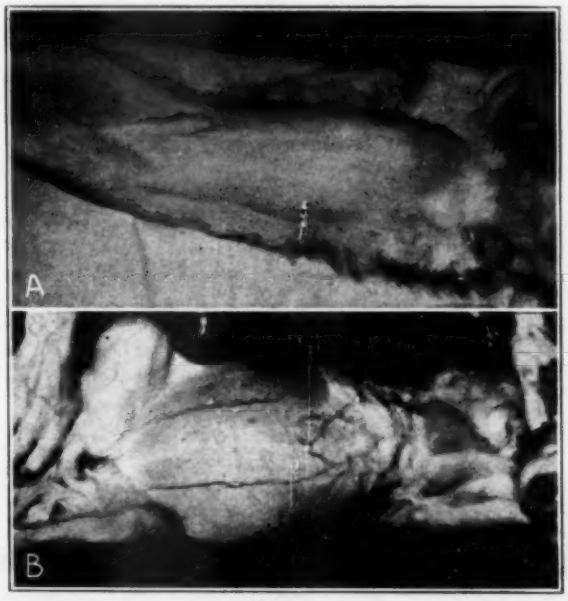

Fig. 2.—Infra-red photographs of 1 normal (*A*) and 1 experimental animal (*B*), showing extensive development of collateral circulation after the production of portal hypertension.

In view of the existence of so efficient a collateral circulation and because of the complicated anatomic arrangement of the hepatic veins in relation to the posterior vena cava, it was decided to try to produce venous portal congestion without associated systemic congestion by a three stage procedure. This method involves ligation of the vena cava immediately caudad to the liver in two stages. By the use of such a procedure, the collateral pathways for returning blood to the heart are allowed to come into full play, thus preventing systemic congestion after the vena cava is completely occluded or severed completely. In the third stage the posterior vena cava anterior to the liver is partially occluded, in this way insuring the development of portal congestion.

METHOD

Dogs ranging in weight between 9.5 and 21 Kg. were anesthetized with pentobarbital sodium administered intravenously. The abdomen was opened by a midline incision and the posterior vena cava exposed. The point of entrance of the adrenorenal veins was located and the cava followed upward under the liver. A ligature was passed around the wall of the cava above the point of entrance of the renal veins and tied (fig. 3, stage I), constricting the lumen of the vessel approximately 70 to 80 per cent. The abdomen was closed in layers. This completed the first stage of the procedure.

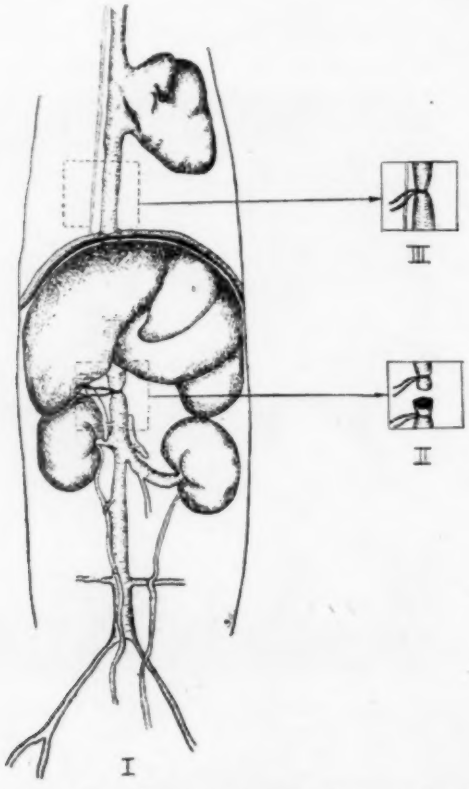

Fig. 3.—Schematic representation of the three stages in the operational procedure for producing venous portal hypertension. Stage II is carried out four or more weeks after stage I, and stage III is done three or more weeks after stage II.

After four weeks or longer the animal was again operated on. The cava was doubly clamped and cut at the site of the partial occlusion. The cut ends of the vessel were ligated with suture ligature (fig. 3, stage II) and allowed to retract as they were dropped back. This step constituted the second part of the procedure.

The third and final stage was carried out three weeks or more after the second stage. With the dogs under intratracheally administered cyclopropane anesthesia, a portion of the ninth rib was resected and the right pleural cavity was opened. The posterior vena cava was identified, and the right phrenic nerve, which runs along with the vein at this point, was dissected free. A ligature was placed around

the cava and tied to occlude the vessel approximately 70 to 80 per cent (fig. 3, stage III). The thoracic wound was closed in layers as the lung was reinflated.

Early in this work an attempt was made to occlude the posterior vena cava between the liver and the diaphragm and thus to avoid entering the pleural cavity, but in several instances in which this step was undertaken it was found that the ligature instead of encircling the cava and the hepatic veins, which are closely associated at this site, actually pierced the vessels. This did not become apparent until autopsies were done on the animals and the exact position of the ligature determined. Because of this uncertainty and other difficulties attendant on ligation of the vessels in this manner, this procedure was abandoned in favor of the one already described.

After the feasibility of the foregoing approach was demonstrated, reference to a similar method, by Soskin and colleagues,[6] was found. These investigators studied the role of the liver in the maintenance of blood sugar level and the movement of sugar into and out of the liver. They prepared the dogs by a preliminary two stage ligation of the posterior vena cava just below the liver. They then measured the blood flow in the thoracic portion of the posterior vena cava and used that as an index of the total blood flow through the liver. In the dogs examined during the present investigations a large diaphragmatic vein emptying into the left hepatic vein at its junction with the third portion of the cava was always found. Thus, not all the caval blood came from the liver.

RESULTS

Forty-six dogs were used in the experiments to be described. The first 3 dogs were used in attempts to produce venous congestion of the liver by ligation directly of the hepatic veins draining the various lobes of the liver. In no instance could a uniform state of congestion be obtained by this method. One dog was subjected to the procedure of Simonds and Brandes [4] for the temporary occlusion of the hepatic veins. The animal was killed with the constricting tube in place in order to obtain precise information concerning the position of the tube and to determine the patency of the posterior vena cava. In 1 dog the vena cava was completely severed and ligated without preliminary partial occlusion. This dog died after twelve hours. In 1 case a lumbar approach to the posterior vena cava was tried and found to be less satisfactory than the intra-abdominal route.

Thirty-nine dogs were subjected to the first stage of the procedure as outlined under the section on methods. Twelve of these died before the second stage. The first animal operated on died of hemorrhage

6. Soskin, S.; Essex, H. E.; Herrick, J. E., and Mann, F. C.: The Mechanism of Regulation of the Blood Sugar by the Liver, Am. J. Physiol. **124**:558 (Nov.) 1938.

from the liver. Of the remaining 11 dogs, 7 had no immediate postoperative complications. In 3 of this group infected wounds developed, which eventually led to their death eleven, nineteen and thirty days after operation, and 2 died of Clostridium welchii infection two and thirty-seven days after operation. Of the remainder, 2 died of distemper, in 1 mange developed and the animal died ninety-six days after operation, 1 was destroyed by fire in the kennels and 1 died of eating poisoned food. None of these deaths could be attributed directly to the circulatory readjustments brought about by occlusion of the posterior vena cava 70 to 80 per cent.

The second stage of the procedure was carried out on 23 dogs. In 2 instances the posterior vena cava had been completely occluded by the first operation. It is, therefore, possible to occlude completely the vena cava without preliminary partial constriction and to have an occasional animal survive. Two dogs died as a direct result of the operation, 1 of hemorrhage from the liver and the other from failure to recover from the anesthetic. Five other dogs died postoperatively: 3 died of Cl. welchii infection five, twelve and fifty-seven days after the stage II operation, and 1 dog died on the ninth postoperative day, after a large hematemesis, but the exact site of bleeding could not be found at necroscopy. In the remaining dog, the attachment of the diaphragm at the ensiform cartilage was cut in making the abdominal incision and a pneumothorax was produced, resulting in death from pneumonia twenty-one days later.

Stages II and III (intra-abdominal method) were combined into one operation in 4 cases. In no instance did the ligature of the cava cephalad to the liver produce the desired effect of constriction by complete encirclement.

The stage III intra-abdominal procedure was carried out as a separate operation on 5 dogs. One died of Cl. welchii infection forty-seven days after the third stage. Necroscopy again revealed that the ligature did not produce constriction. An interesting and most unusual finding in this animal was a small canalized endothelial tube containing blood, which had bridged a gap of 2 cm. between the cut ends of the severed vena cava. Two dogs died one and ten days after stage III, from hemorrhage from the vena cava and the liver. In both animals the ligature had passed through the lumen of the posterior vena cava and not around the vessel. In 1 dog there was considerable bleeding from a torn hepatic vein; this was controlled by ligature, and the animal survived. Because of the results obtained, the intra-abdominal route for stage III was abandoned and it was decided to constrict the cava cephalad to the liver in the thorax.

The thoracic approach to the posterior vena cava was attempted on 8 animals. Three dogs died on the operating table, from the anesthetic.

The remaining 5 dogs were successfully operated on, and the posterior vena cava constricted approximately 70 to 80 per cent in the thorax, immediately cephalad to the diaphragm. One of the dogs died of empyema six days after the last operation. The 4 remaining dogs survived for much longer periods and were used in extensive physiologic and chemical studies. The dogs all showed pronounced development of the collateral veins on their ventral aspect. Figure 2 shows 1 normal and 1 experimental animal as viewed by infra-red photography. One of these dogs died three months after the stage III operation. The animal did well up to about a week before it died; at that time it became progressively weaker and more sluggish until it finally expired. Necroscopy showed the posterior vena cava in the thorax almost completely occluded. The kidneys appeared mottled, the spleen small and the stomach dilated. In another one of these dogs a large ventral hernia developed. The animal was anesthetized with open drop ether in order that this hernia might be repaired and it died as a result of anesthesia before any operation was carried out. This was almost seven months after the stage III operation. At necroscopy it was found that the encircling ligature constricted the thoracic portion of the posterior vena cava about 60 per cent. The azygous vein was almost as wide as the vena cava. The liver was normal in size; it was dark in color (bluish black) and adhered to all the surrounding viscera; in section it was gritty. The pancreas was normal and the spleen smaller than normal, with no adhesions. The stomach was small. The small intestine adhered to the dorsal part of the abdominal wall. The veins in this region were extremely distended. The kidneys appeared congested, although the renal veins were normal in size. The two remaining dogs were killed after all the physiologic experiments were completed.

COMMENT

A procedure has been devised for production of venous congestion in the dog mechanically, a three stage operation being used. This method, in contrast to earlier methods, has the advantage of avoiding the congestion of systemic regions caudad to the occlusion. It does so by taking into account the complex nature of the relationship between the hepatic veins and the posterior vena cava and by making use of the collateral circulation from the caudal regions of the body to the heart, in this way preventing caudal congestion.

That portal hypertension occurs in animals subjected to the operational procedure described has been noted in extensive physiologic studies carried out on many of the dogs and especially on the 4 animals that survived all the operations. These studies, together with chemical analysis, will be reported on in detail in a forthcoming publication. However, some of the more general effects of the operational procedures

will be discussed at this time. The portal pressure is increased after the first operation. By partial occlusion of the postcaval vein caudal to the liver increased portal resistance is built up and the blood is forced into channels which are inconspicuous under normal conditions. These anastomoses connect the portal and systemic veins and thereby promote a path for the return of blood from the splanchnic area to the right side of the heart.

After the new collateral circulation has developed stage II can be performed, with minimum damage to the kidneys.

With the performance of stage III the portal blood pressure is increased still more. With an original pressure of about 8 cm. of water, there is no filtration from the capillaries into the abdominal viscera. With increased pressure of 15 cm. or more of water, there is increased filtration. The slow rise in pressure is evidenced by the latent period of the development of ascites after the posterior vena cava has been partially occluded below the heart. Ascites in these animals was not observable until seven to twenty days postoperatively. Increasing quantities of ascitic fluid were formed as measured by changes in weight and by the large quantities of fluid that could be withdrawn.

SUMMARY

1. The anatomic relationships between the hepatic veins and the posterior vena cava in the dog are described.

2. A method for the mechanical production of venous congestion of the liver and accompanying portal hypertension has been devised.

Valuble help and cooperation in this work were received from Dr. Donal Sheehan, Professor of Anatomy, and Dr. Frank W. Co Tui, Associate Professor of Experimental Surgery.

CARCINOMA OF PANCREAS STILL LOCAL AT AUTOPSY FOUR YEARS AFTER PALLIATIVE OPERATION

HARRY C. SALTZSTEIN, M.D.
AND
JOHN RAO, M.D.
DETROIT

Mattie A., aged 38, was admitted to Mercy Hall Cancer Hospital on March 9, 1945. She had been operated on at Woman's Hospital by Dr. W. E. Johnston in July 1941. Dr. Johnston, Dr. Don M. Beaver and Dr. Frances Ford supplied the notes from the latter hospital admission.

Prior to her admission to Woman's Hospital the patient had complained of pain and tenderness underneath the right costal margin for one year and of jaundice for two weeks. She had weighed 90 pounds (40.8 Kg.) and had a hemoglobin content of 60 per cent and a red blood cell count of 3,250,000.

At abdominal exploration on July 25, 1941, the head of the pancreas had been found to be the size of a large plum, round and hard. The gallbladder had been distended and the common duct dilated. There had been no evidence of disease of the gallbladder.

Cholecystogastrostomy had been done and a specimen for biopsy taken from the pancreas. Microscopic examination had revealed a "new growth consisting of anaplastic epithelial cells having a ductal differentiation. The diagnosis was adenocarcinoma of the head of the pancreas (ductal in type) of malignancy grade 2" (fig. 1).

The jaundice had disappeared twenty-one days after the operation and the patient had gone home. She had evidently been fairly well for three and a half years since the operation, was doing her own housework and felt strong. However, during the past eight months, i. e., since August 1944, she had failed. There had been edema of the legs since July 1944. She had not eaten well and had lost 40 pounds (18 Kg.). She had evidently been on a deficient diet in that she never ate any fruit or drank any milk.

General examination on admission to Mercy Hall Cancer Hospital on March 9, 1945 revealed a thin, emaciated woman. Abdominal examination was noncontributory except for scars of a previous laparotomy.

A blood cell count showed moderate anemia, a red blood cell count of 3,200,000, with 62 per cent (10.5 Gm. per hundred cubic centimeters) hemoglobin, and a white blood cell count of 6,300. Roentgenograms revealed a defect in the pyloric portion of the stomach, close to the duodenum, which was thought to be due to pressure from an extragastric mass. The stomach itself showed no intrinsic lesion.

Her course in the hospital was further downgrade. She appeared mentally deficient, said many foods were not good for her and seemed lethargic, weak and not interested in her surroundings; she died three weeks after entrance, on April 29, 1945.

From Mercy Hall Cancer Hospital and Tumor Clinic.

Autopsy revealed a large adenocarcinoma involving the head and midportion of the pancreas (fig. 2). It was a nodular grossly spherical tumor mass 8 by 10 cm. in diameter but was entirely local and could be shelled away from the smaller distal portion, or tail, of the pancreas. When removed, it left the bed of the pancreas clean and free; there were no fixed extensions which would have prevented resection, and there were no local or distant metastases.

Fig. 1.—Biopsy specimen of carcinoma of the pancreas obtained at laparotomy on July 25, 1941. Cholecystenterostomy was done. The patient lived in relative comfort for four years.

Microscopic examination revealed adenocarcinoma somewhat more malignant than that shown in the biopsy specimen taken at laparotomy in 1941 but still easily recognizable as the same cell type (fig. 3).

SUMMARY

A case of carcinoma of the pancreas is presented which was proved by laparotomy and biopsy in 1941. In 1945, autopsy showed the tumor still local and apparently (as far as appearances at autopsy went) still resectable.

COMMENT

Carcinoma of the pancreas is notoriously a disease of short duration from the onset of the symptoms to death. The total lapse of time between these two events is given as six months (Cecil [1]), six to eighteen months (Cyclopedia of Medicine, Surgery and Specialties [2]), six to eight months

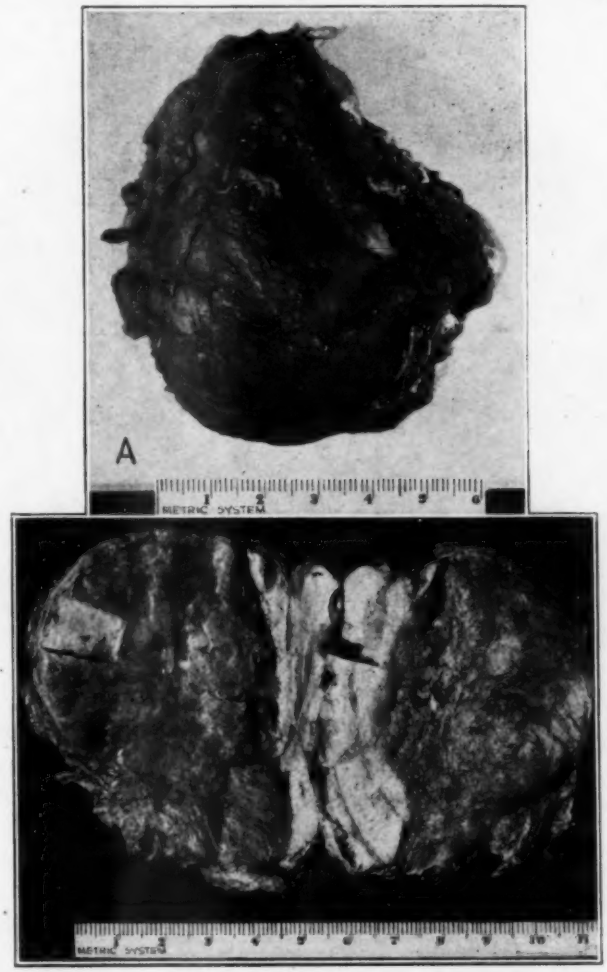

Fig. 2.—*A*, outer surface of a tumor of the pancreas removed at autopsy April 29, 1945. It involved the head and midportion of the pancreas and could be shelled out, leaving a clean bed without local extention. There were no metastases. *B*, cut section of the tumor.

1. Cecil, R. L.: Text-Book of Medicine, Philadelphia, W. B. Saunders Company, 1943, p. 979.

2. Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1945, vol. 11, p. 120.

(Brunschwig [3]) and five to eight months, with the longest two years (Rives and colleagues [4]).

Ransom [5] reviewed 109 cases of cancer of the pancreas at the University Hospital of the University of Michigan Medical School in 1938. The average duration of symptoms before admission was five and one-half months, and the average length of life after palliative operation in

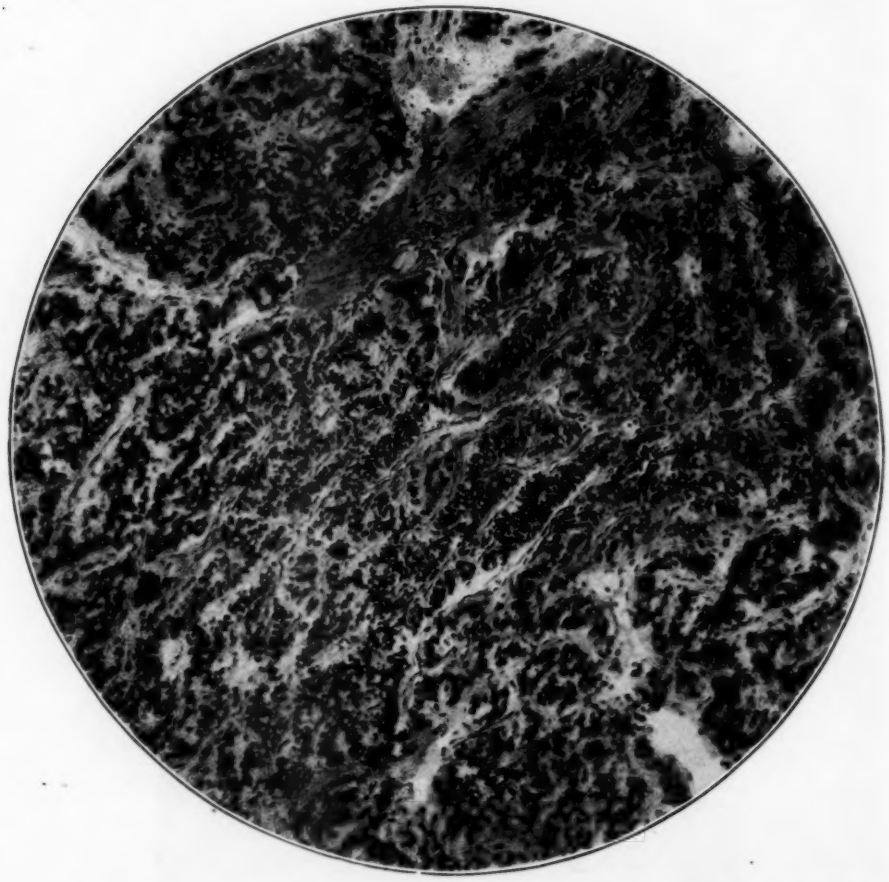

Fig. 3.—Microscopic section (autopsy specimen) of the tumor. Note similarity with figure 1.

3. Brunschwig, A.: Radical Resections of Advanced Intra-Abdominal Cancer, Ann. Surg. **122**:923 (Dec.) 1945.

4. Rives, J. D.; Romano, S. A., and Sandifer, F. M., Jr.: Carcinoma of Pancreas, Surg., Gynec. & Obst. **65**:164 (Aug.) 1937.

5. Ransom, H. K.: Carcinoma of Pancreas and Extrahepatic Bile Ducts, Am. J. Surg. **40**:264 (April) 1938.

cases in that institution by a previous report (Coller and Winfield, 1934 [6]) was 7.2 months.

Ransom stated: "In view of the notoriously rapid progress and relatively short life history of the disease, the histories of illness lasting over one year are perhaps open to question. In such instances it is quite possible that symptoms antecedent, such as gallbladder disease and peptic ulcer, may have merged with the earliest symptoms of cancer." He further stated that "long periods of relief of symptoms [following palliative operations] are occasionally reported. In such cases one is driven to the conclusion that the mass felt at the time of the operation was in fact inflammatory rather than neoplastic and that the internal drainage of the biliary tract resulted in a permanent cure."

Lahey [7] stated, "Many of these patients live comfortably for several months [following palliative short-circuiting operations] and occasionally two or three years before dying from the slow-growing carcinoma within the head of the pancreas." But, he added, "The length of time over which some of the patients upon whom we have done cholecystenterostomy for jaundice have lived can be explained . . . only by the fact that in some of the cases the obstruction was benign in character." Other authors have similarly expressed the feeling that in cases of long time arrests the obstructions were probably benign conditions rather than cancer.

We have not been able to find a proved case of carcinoma of the pancreas in which the patient lived four years after operation, such as happened in this patient. There are, however, occasional reports of cases of carcinoma of the pancreas which was still local at time of autopsy and in which, as far as gross autopsy appearances went, a radical resection might have been done.

Gordon-Taylor [8] stated, "In one case of my own, for which three palliative operations (!) of diverse nature had already been performed at another institution during the previous fifteen months and in which the diameter of the tumor was nearly 3½ in., the affected portion of the head of the pancreas was found at necropsy still to retain motility and showed no involvement of the portal vein or its parent tributaries, and there were no metastases."

In Ransom's series, in 30 autopsies five tumors originating in the biliary ducts were still localized, while two pancreatic cancers, one in

6. Coller, F. A., and Winfield, J. M., Jr.: Evolution of Palliative Operation for Cancer of the Pancreas, Am. J. Surg. **25**:64 (July) 1934.

7. Lahey, F.: Carcinoma of the Pancreas, S. Clin. North America **17**:753 (June) 1937.

8. Gordon-Taylor, G.: The Radical Surgery of Cancer of the Lower End of the Common Bile Duct and Adjacent Pancreas, Brit. M. J. **2**:119 (Aug. 1) 1942.

the head and one in the body, were still local. Hick and Mortimer,[9] in 50 cases that came to necropsy, found 3 cases in which no metastases were found. These were cases of scirrhous carcinoma of the head of the pancreas. Rives and colleagues reported that 8 out of 96 patients were found at necropsy to have localized and resectable lesions.

The lesson clearly is that, with modern surgical improvements in technic and availability of large amounts of blood, there is a wider scope for operative removal. Involvement of the stomach, duodenum, middle colic vessels and even a portion of the portal vein are not absolute contraindications to wide removal. Such resections represent an attempt at cure or long time arrest, not palliation for a few months.

9. Hick, F. K., and Mortimer, H. M.: Carcinoma of the Pancreas, J. Lab. & Clin. Med. **19**:1058 (July) 1934.

PARA-ARTICULAR OSSIFICATION OF THE SOFT PARTS OF THE ANKLE

Complication of Sprain With or Without Fracture of the Shaft of the Ipsilateral Fibula

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IN 6 CASES of sprained ankle my colleagues and I noted the association of recurrent protracted episodes of pain and swelling of the part with ossification of local para-articular tissue.[1] In addition, there were 2 cases of sprain of the ankle with similar complications coexistent with fracture of the shaft of the ipsilateral fibula.

The clinical and roentgenographic findings in these 8 cases are presented to show the development of para-articular ossification about the region of the ankle and to stress its frequency.

HISTORY AND SYMPTOMS

Three soldiers (group A), from 18 to 35 years of age, who came under our observation immediately after the advent of sprain of the ankle, experienced unusual prolonged convalescence. While a group of 42 other patients with sprain of the ankle made almost complete recoveries in from four to six weeks on routine treatment,[2] these 3 patients

1. Benassi, E.: Ossificazione post-traumatica paratibiale, Arch. di ortop. **45**:409-415, 1929. Bistolfi, S.: Contributo allo studio della ossificazioni traumatiche para-articolari: le ossificazioni para-malleolari, Arch. di radiol. **8**:566-604, 1932; Ulteriori osservazioni sulle ossificazioni post-traumatiche para-malleolari, con speciale riguardo alla diagnosi differenziale colle fratture parcellari, ibid. **9**:1061-1081, 1933. Köhler, A.: Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram, ed. 2, Baltimore, William Wood & Company, 1935. Pellegrini, A.: Ossificazioni post-traumatiche pararticolari (O.P.P.), Arch. ital. di chir. **53**:501-563, 1938. Hempel, C.: Schalenförmiger Abbruch an der hinteren unteren Tibiafläche oder Verkalkung des Ligamentum malleoli lateralis posterius? Deutsche Ztschr. f. Chir. **258**:100-102, 1943. Brailsford, J. F.: The Radiology of Bones and Joints, ed. 3, Baltimore, Williams & Wilkins Company, 1944. Piatt, A. D.: Post-Traumatic Para-Articular Calcifications and Ossifications of the Ankle, Am. J. Roentgenol. **54**:348-356, 1945.

2. Treatment of simple sprain consisted in rest in bed and the application of cold compresses to the ankle for three to seven days. This was followed by a course of hydrotherapy, active exercises and weight bearing for periods from thirty to forty-five days. A rocker-bottom shoe was prescribed for at least the first thirty days of weight bearing. In instances in which complete tear of the fibuloastragalar ligaments was demonstrated by roentgenographic studies of the inverted astragalus, immobilization in plaster of paris boots was carried out.

complained of recurrent pain and swelling of the part from four to seven months after the onset of the sprain—the duration of the follow-up period. The injuries sustained by these 3 appeared to be similar in degree of severity to those suffered by the other 42 soldiers.

There were 3 other soldiers (group B), not included in the series of 42 patients, who also sought treatment for complaints of recurrent swelling and pain of a single ankle. They had suffered from sprain of the ankle from two to three years prior to their first visit to the orthopedic clinic.

Two soldiers (group C) who suffered from fracture of the shaft of the fibula with accompanying sprain of the ipsilateral ankle also complained of the pain and swelling of the joint before and after the removal of the plaster of paris boots. These symptoms reappeared several months after the occurrence of the sprain, in spite of hydrotherapy, graded exercises and limited activities.

PHYSICAL EXAMINATION

The examination of the 3 patients (group A) made soon after the onset of sprain of the ankle revealed the usual findings of ecchymosis, obliteration of landmarks by swelling, diffuse tenderness over the region of the ligaments and slight restriction in the range of active and passive movement of the foot. Reexamination of these 3 patients at intervals of one week for thirty-five days demonstrated the persistence of effusion, obliteration of landmarks, tenderness over the region of the posterior ligaments of the ankle and totals of 5 to 10 degrees of restriction in both active and passive dorsiflexion and plantar flexion of the foot. Examinations of these 3 patients (group A) made from four to seven months after the initial injuries disclosed moderate enlargement of the ankle and tenderness either on its medial or on its posterior surface. A total of 5 to 10 degrees of restriction in active and passive dorsiflexion and plantar flexion of the foot was again observed. Reexamination, made approximately four or more months after the sprain, revealed that avoidance of weight bearing for one or two days resulted in partial disappearance of the pain and swelling of the ankle. Recurrence of these symptoms was prompt after a short period of marching or hiking.

Examination of the 3 other patients (group B), who had suffered from recurrent swelling of an ankle for the past two to three years, disclosed partial obliteration of the normal landmarks, localized tenderness over the region of the posterior ligament of the affected part and totals of about 5 to 10 degrees of restriction in active and passive dorsiflexion and plantar flexion of the foot. On complete rest of the affected extremity for one or two days, the ankle presented almost normal appearance.

Examination soon after injury of the 2 patients with fracture of the shaft of the fibula (group C) revealed ecchymosis, swelling and tender-

ness of the leg as well as enlargement of the ipsilateral ankle. Movements at the ankle were painful and were restricted for totals of 10 to 25 degrees in active and passive dorsiflexion and plantar flexion of the foot. Reexamination made soon after the removal of the plaster of paris boots, from fifty to sixty days after the injury, disclosed moderate enlargement of the ankle. Localized tenderness was present over the posterior, lateral and medial aspects of the ankle. Follow-up studies made four or more months after the injuries disclosed that after complete rest of the extremity for one or two days there was a partial resolution of the swelling of the ankle. These 2 patients suffered considerably more from the swelling in the ankle than from the fracture of the shaft of the fibula.

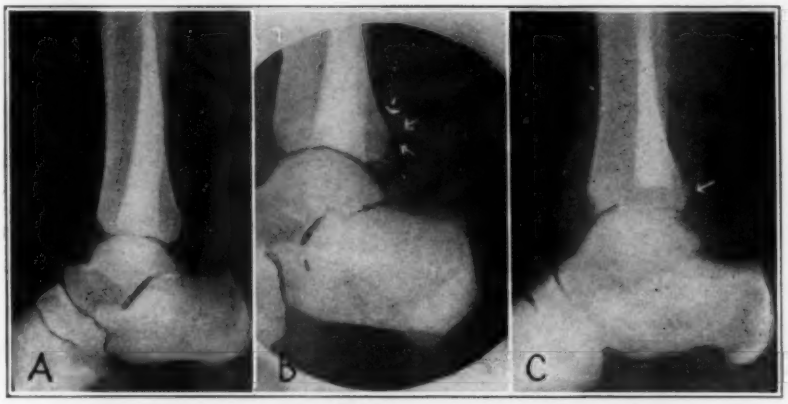

Fig. 1.—*A*, a roentgenogram taken soon after the occurrence of the sprain reveals swelling of the soft tissues of the region of the ankle (group A). *B*, a roentgenogram of the same ankle taken forty days later reveals an opaque plaque in the region of the posterior ligament (arrows). *C*, a roentgenogram of another ankle shows an opaque plaque in the region of the posterior ligament. This shadow made its appearance fifty days after the sprain (group A).

ROENTGENOGRAPHIC EXAMINATION

Roentgenographic studies made of the ankles of 3 patients (group A) soon after the occurrence of sprain showed no significant changes except local swelling of the soft tissues (fig. 1 *A*). Roentgenograms taken subsequently of these 3 patients, from forty to sixty days after sprain, demonstrated in each instance the presence of a small, thin vertical plaque of increased density in the region of the inferior transverse or posterior ligaments, just posterior to the distal extremity of the tibia. A clear or radiolucent zone existed between this area of increased density and the cortex of the tibia (fig. 1 *B* and *C*). In 2 of these 3 patients, areas of increased density were also present at this time in the

interosseous ligament, just proximal to the distal fibulotibial articulation. Roentgenograms of these parts taken from three to six months after the advent of the sprain revealed slight increase in the size and density of the radio-opaque shadows located in the interosseous and posterior ligaments. None of these opaque foci became attached to the fibula or tibia. These 3 soldiers presented no evidence of fracture, separation or subluxation of the bones comprising the ankle joint.

In addition, we had an opportunity to study roentgenographically 3 patients (group B) who had complained of swelling of the ankle for the past two to three years. Roentgenographic examination made of these 3 patients from two to three years after the initial sprain also demonstrated the existence of linear or elliptic-shaped plaques of increased density in the soft parts in the region of the distal end of the

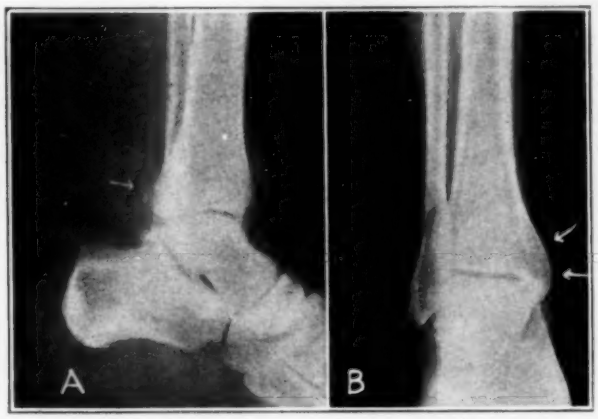

Fig. 2.—*A*, a roentgenogram of ankle reveals an opaque plaque in region of the posterior ligament. The patient (group B) has had recurrent local pain and swelling following a sprain of the ankle two years before. *B*, a roentgenogram of another ankle shows two opaque plaques in the region of the medial ligament. The patient (group B) has also experienced recurrent pain and swelling of the part for the past three years.

tibia. Two of these 3 soldiers presented densities which were situated in the vicinity of the inferior transverse or posterior ligaments (fig. 2 *A*). Roentgenograms of the ankle of the third patient revealed the presence of linear plaques of increased density in the para-articular region of the inner aspect of the medial malleolus of the tibia (fig. 2 *B*).

Another group, of 2 patients (group C), with fracture of the distal third and the upper third of the fibula respectively, also presented evidence of accompanying sprain of the ipsilateral ankle. Each of these 2 patients was immobilized in a plaster of paris boot for a period from fifty to sixty days. Within thirty days after the fracture of the lower third of the fibula, an opaque plaque was seen to form in the soft parts in

the locale of the inferior transverse or posterior ligaments of the ankle joint. In the other soldier, in whom the fracture had occurred at the upper third of the fibula, opacities were observed in the neighborhood of the inferior transverse or posterior ligament of the ankle within forty days after the initial injury. The formation of extra-articular bone in these 2 subjects was encountered during the period of immobilization of the leg and foot in the plaster of paris boot.[3]

TREATMENT

No attempt was made to remove the opaque plaques by surgical intervention. The soldiers in question were reassigned to duties which did not entail excessive walking or marching. They wore elastic bandage supports about the ankle and received repeated courses of hydrotherapy. This plan of treatment plus change in the status of duty resulted in definite partial resolution of the swelling and alleviation of the pain. In no instance, however, did the treatment which we pursued cause a disappearance of the radio-opaque plaques in the para-articular region of the ankle. The maximum period of follow-up of these 8 soldiers was twelve months.

COMMENT

The formation of dense plaques in the ligamentous structures about the ankle appears to be similar in character to that which takes place in the region of the tibial collateral ligament of the knee after trauma. Although para-articular ossification of the extremities may develop secondary to lesions of the spinal cord or of the peripheral nerves, no neurologic disturbances were present in these 8 patients.[4] We postulate that the complication described in this study is the result of ossification and not calcification of the connective tissue. This is not due to new periosteal bone but is probably secondary to healing of partly torn or stretched fibers of connective tissue about and in the ligaments of the ankle as well as in the interosseous ligament binding the fibula to the tibia. In 1 of the 8 patients, in whom a fracture had occurred at the upper third of the fibula in conjunction with a sprain of the ipsilateral ankle, the roentgenographic study of the ankle showed two distinct coexisting lesions (fig. 3). Firstly, a linear opaque plaque was noted

3. In another case of fracture of the fibular shaft and of the posterior margin of the distal end of the tibia with an incompletely fractured inner malleolus, we noted on roentgenograms made soon after the injury two linear spicules of bone detached from the cortex of the inner malleolus. This must be differentiated from para-articular ossification, which occurs approximately thirty or more days after the injury.

4. Sutro, C. J., and Pomerantz, L.: Effect of Experimentally Formed Tumors on Musculoskeletal System of Rat, Arch. Surg. **38**:1132-1149 (June) 1939.

in the region of the posterior ligament of the ankle, and secondly, formation of new periosteal bone was observed on the medial malleolus. This finding demonstrated that new periosteal bone caused by irritation of the periosteum can be differentiated roentgenographically from formation of para-articular bone.

The possibility that active movement of the affected ankle soon after the injury provoked formation of extra-articular bone can be ruled out. In 2 cases of fracture of the fibula with sprain of the ipsilateral ankle, we observed the formation of bone in the region of the posterior and medial ligaments during the period in which the affected leg and foot were immobilized in a plaster of paris boot.

As for the basis of the recurrent swelling of the ankle, we suspect that ossification in the region of the para-articular tissues caused secon-

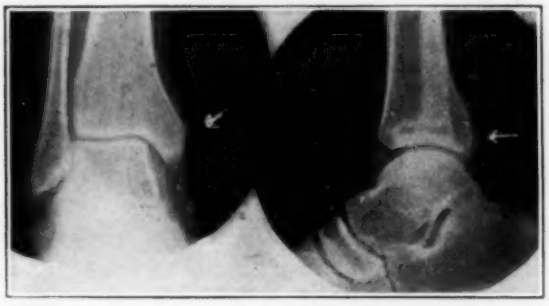

Fig. 3.—A roentgenogram of an ankle (group C) reveals in the anteroposterior view formation of new periosteal bone on the inner malleolus. The lateral view shows a dense plaque in the region of the posterior ligament. Note the clear space between it and the cortex of the tibia.

dary inflammatory or irritative changes on the synovial surfaces of the contiguous capsules.

SUMMARY AND CONCLUSION

In 3 soldiers with protracted local pain and swelling of the ankle as the result of simple sprain of the part, we observed on roentgenographic study the formation of thin radio-opaque plaques in the region of the inferior transverse and posterior ligaments of the ankle. In 2 of these 3 patients, additional foci of ossification were noted in the vicinity of the interosseous ligament. These changes occurred under observation from forty to sixty days after simple sprain of the soft parts of the ankle.

In 3 other patients, in whom recurrent pain and swelling of the ankle had been present for two or three years after simple sprains, we noted on roentgenographic examination similar plaques of increased density in the region of the posterior or medial ligaments of the ankle.

Furthermore, in 2 other patients, with sprain of the ankle coexistent with fracture of the shaft of the ipsilateral fibula, similar developments of opacities in the region of the posterior ligament of the ankle were also observed.

Ossification of the connective tissue about and in these ligaments probably irritates the contiguous synovial lining of the ankle joint, with resultant effusion.

While ordinary sprain of the ankle usually affects the fibuloastragalar ligaments, it may also cause tears of parts of the interosseous ligament as well as of the inferior transverse, medial or posterior ligaments without resultant separation at the distal fibulotibial articulation. When such sprain is complicated by para-articular ossification, recurrent effusion and pain of the ankle may be intermittently present. Limitation of activity of the limb with the aid of a support about the ankle caused a partial resolution of the swelling and pain.

The clinical and roentgenographic picture of these 8 patients with para-articular ossification of the soft parts of the region of the ankle appears to be similar for the most part to that of ossification of the tibial collateral ligament of the knee.

INJURIES OF THE THORACIC DUCT

Report of a Case of Chylothorax in Which the Patient Recovered After Ligation of the Thoracic Duct

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CHYLOTHORAX due to damage of the thoracic duct either in the neck or in the chest is of rare occurrence and carries a high mortality. The continuous loss of chyle, without replacement, results fatally. Shackelford and Fisher [1] in 1938 summarized the findings in 41 completely recorded cases collected up to that time. Seven additional cases were not included in their statistical study, because of insufficient data. The mortality was 47.5 per cent. Bauersfeld [2] in 1937 could find only 6 cases reported from this country. Dorsey and Morris [3] in 1943 added 12 more cases, bringing the total to 60, and in 1945 Florer and Ochsner [4] reported another; including the case reported in this paper, the total is in the neighborhood of 62.

While chylothorax is of rare occurrence, severance of the thoracic duct in the neck without chylothorax is not uncommon. On one occasion, I deliberately ligated the duct in doing a radical dissection of the neck for carcinoma of aberrant thyroid tissue, without ill effect, and I have had reports from other doctors on 3 cases in which injury occurred at the time of operation and was recognized. In 1 instance the duct was ligated following its injury while a deep-seated gland was being removed for biopsy. In another, it was sutured following a partial severance while the anterior scalene muscle was being cut. In the third case, an anastomosis to the proximal stump of the internal jugular vein was done following its severance in a radical dissection of the neck. In none of these cases was there any complication from the ligation of the duct.

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1. Shackelford, R. T., and Fisher, A. M.: Traumatic Chylothorax, South. M. J. **31**:766 (July) 1938.

2. Bauersfeld, E. H.: Traumatic Chylothorax from Ruptured Thoracic Duct Treated by the Intravenous Injection of the Aspirated Chyle, J. A. M. A. **109**:16 (July 3) 1937.

3. Dorsey, J. F., and Morris, G. E.: Traumatic Rupture of the Thoracic Duct with Chylothorax, J. A. M. A. **119**:337 (May 23) 1942.

4. Florer, R., and Ochsner, A.: Traumatic Chylothorax, Surgery **17**:622 (April) 1945.

ANATOMY

The thoracic duct originates from the cisterna chyli at about the second lumbar vertebra, passes through the aortic hilus of the diaphragm, lying between the aorta and the azygos vein, and ascends in the same relative position, slightly to the right of the midline, crossing to the left at the junction of the last cervical and the first thoracic vertebra.[5] It ascends into the neck behind the carotid sheath, rising as high as 2¼ inches (6 cm.) above the upper border of the sternum, and then curves downward to enter the subclavian vein near its junction with the internal jugular vein. Its location in the neck is not constant, and the frequent variations should keep the surgeon operating in the left side of the lower part of the neck constantly on his guard. The primitive ducts were phylogenetically paired right and left vessels that ascended the posterior mediastinum and emptied into both the right and the left subclavian vein. Numerous cross communications existed and subsequently atrophied, the somewhat devious thoracic duct remaining as the main channel. The embryonal remains probably play a part in the collateral circulation that develops after ligation of the duct.

It is often erroneously thought that ligature of the thoracic duct at the point of venous entrance accomplishes complete obstruction and will result fatally. Harrison[6] in 1916 cautioned against ligature and described a method of anastomosing the duct to a nearby vein. However, De Forest,[7] as early as 1907, advised its ligature, stating his belief that adequate collateral circulation developed. Lee[8] in 1922 reviewed the subject and demonstrated in animals an extensive collateral circulation. The rerouted chyle may enter the circulation through a right thoracic duct or through connections with the azygos or intercostal veins. Lee also observed lymphatic connections in the abdomen with the lumbar veins. Connections have also been reported in other abdominal veins, such as the renal and the mesenteric. It is actually extremely difficult to exclude entirely the entrance of chyle into the venous system. In 1937, Blalock and his associates[9] tried a variety of operations on some 74 animals and were able to produce

5. Grant, J. C. B.: Method of Anatomy, ed. 3, Baltimore, Williams & Wilkins Company, 1944.

6. Harrison, E.: On the Treatment of Wounds of the Thoracic Duct, Brit. J. Surg. **4**:304, 1916.

7. De Forest, H. P.: The Surgery of the Thoracic Duct, Ann. Surg. **46**:705, 1907.

8. Lee, F. C.: The Establishment of Collateral Circulation Following Ligation of the Thoracic Duct, Bull. Johns Hopkins Hosp. **33**:21 (Jan.) 1922.

9. Blalock, A.; Robinson, C. S.; Cunningham, R. S., and Gray, M. E.: Experimental Studies on Lymphatic Blockage, Arch. Surg. **34**:1049 (June) 1937.

complete blockage in only 3. From this discussion, it is evident that ligation of the thoracic duct is not a dangerous procedure. It is the continuous external loss of chyle that results fatally.

The importance of the thoracic duct has been recognized for well over a century. Among the functions of the lymph system is the transport of 60 to 70 per cent of the fat from the lacteals of the intestinal villi into the venous system. As chyle is a filtrate, it might be expected that its other constituents would resemble those found in blood serum. This is true, but in amounts usually smaller than in serum. The protein content varies between 1 and 6 Gm. per hundred cubic centimeters. Sugar, nonprotein nitrogen, urea and amino acids are about the same as serum. The cholesterol and calcium contents are perhaps slightly lower. Lymph also clots, but more slowly than serum, as the thromboplastin derived from blood platelets is poorly represented and there is a relative excess of antithrombin.

As it has been shown that lymph flow may range from 60 to 190 cc. per hour in the thoracic duct, depending on circumstances,[10] a tremendous loss of fluid and important body constituents may take place in a twenty-four hour period. Pressures in the thoracic duct vary and are influenced by such things as intraperitoneal pressure, intrathoracic pressure, inflammation and food but are higher than venous pressures, which promote the ready entrance of lymph into the veins at the base of the neck. On complete blockage of the duct high pressures develop, but they fall after the development of collateral circulation. Another function of the lymph system has been indicated by Co Tui and his associates.[11] In 1944, they demonstrated that it is an important pathway not only for the return of proteins from the capillary filtrates to the blood but also for the mobilization of proteins from depots in the body and therefore is an important aid in maintaining the volume of blood and proteins following hemorrhage.

Chylothorax may result from a variety of injuries which either directly or indirectly result in tears or severance of the thoracic duct.[12] In the order of frequency, the following were the causes in the 41 cases summarized by Shackelford and Fisher: crushing injuries, wounds by bullet or stab, fall from a height, blow on the chest, throw against the front seat of an automobile or sudden hyperextension. Injury following a full meal seems to be of some importance. Accumu-

10. Drinker, C. K., and Yoffey, J. M.: Lymphatics, Lymph and Lymphoid Tissue, Cambridge, Mass., Harvard University Press, 1941.

11. Co Tui; Barcham, I., and Shafiroff, B. G. P.: Ligation of the Thoracic Duct and the Posthemorrhage Plasma Protein Level, Surg., Gynec. & Obst. **79**:37 (July) 1944.

12. Smith, D. D., and Woliver, E.: Traumatic Chylothorax, Arch. Surg. **43**:627 (Oct.) 1941.

lations of fluid on the right side are most frequent and commonly result from indirect injury, the site of break usually being just above the diaphragm. The slightly right-sided position of the duct in the greater part of the chest is given as the reason for this. Bilateral chylothorax and association with chylous ascites have also been reported. Left-sided collections of lymph indicate an injury high in the duct.

In such thoracic operations as lobectomy, esophagectomy, rib resections for tumor or a Smithwick procedure, the position of the thoracic duct should be kept constantly in mind. Operations involving the left side of the lower part of the neck frequently endanger the thoracic duct.

The symptoms resulting from leakage of chyle are of two general types: those due to pressure and those due to loss of lymph chyle. If the duct is injured in the chest, pressure symptoms at first predominate, to be followed by the symptoms produced by the loss of large amounts of chyle. Dyspnea is usually the first indication that fluid is accumulating in the chest. This may be delayed twenty-four hours or several days, explainable on the basis of the fluid being first confined to the posterior mediastinum and later breaking through into the pleural cavity.

The continuous loss of chyle produces the symptoms expected from the escape of large quantities of fluid, rich in the same constituents as blood serum and, in addition, fat. Weakness, hunger and thirst develop. In a comparatively short time emaciation and inanition become striking features. There is a decrease in urinary output. The pulse becomes weak and rapid. Apathy supervenes, and death by starvation occurs in about three weeks.

Diagnosis may at first be confusing owing to a concomitant hemothorax. After repeated tappings, the fluid clears and its true character can be recognized. It is milky in appearance and, on standing, separates into three layers: cream on the top; a second, milky, layer; and a lower layer, of cellular sediment. Lymph is alkaline in reaction and has a specific gravity of 1.012 or higher. Its white count may vary from 2,000 to 20,000 cells per cubic millimeter. Lymphocytes predominate, with a few eosinophiles, transitionals and unclassified cells. A few red cells are also usually present. As a result of the loss of lymphocytes in the chyle there is a drop in the lymphocyte count in the blood. Accompanying the large loss of chyle there is a general drop in the blood proteins and calcium.

REPORT OF A CASE

A patient, an army lieutenant, was received aboard a Navy hospital ship at Saipan, three days after being wounded. He was poorly oriented as to

time and place and in evident respiratory distress. The left side of the chest was splinted, and the patient was expectorating a dark, bloody sputum. While he had multiple superficial wounds, the essential wound had been caused by a bullet entering the left scapular area at the level of the third rib and leaving in the left supraclavicular area, 2 cm. from the midline and 1 cm. above the clavicle. These were reported to have been sucking wounds, and both had been sutured on the beach. Thoracentesis yielded from the left side of the chest 500 cc. of air and 650 cc. of blood. This was followed by pronounced improvement in respiration and pulse. Twenty-five thousand units of penicillin was instilled into the pleural cavity, and the administration of sulfathiazole was started by mouth. Plasma and fluids were given intravenously. The following morning, increasing respiratory embarrassment required another thoracentesis, at which time 950 cc. of bloody fluid was removed. Twice daily, taps were necessary to relieve the dyspnea.

By the fourth day after admission the fluid became a lighter red, and because of the line of flight of the bullet my colleagues and I became suspicious of chylothorax, with injury to the thoracic duct just above the clavicle. It was not until the fifth day that the true character of the fluid became apparent, as shown by its milky appearance and the presence of fat globules. Between 1,700 and 2,400 cc. of chylous fluid was removed daily. The patient was given at least 2 units of plasma daily, together with 2,000 cc. of 5 per cent dextrose and isotonic solution of sodium chloride and placed on a low fat, high protein diet. Despite this therapy his condition became progressively worse. He was listless and apathetic. His cheeks and eyeballs were sunken, and he had the general emaciated appearance of a starving person. It was decided that continued medical management would be fruitless and that operation offered the only chance for recovery.

Laboratory Work Before Operation

7/9/44	Red blood cells	5,080,000
	White blood cells	10,500
	Hemoglobin	75 per cent
	Hematocrit	46 per cent
	Proteins	5.1 mg. per 100 cc.
	Whole blood chlorides	445 mg. per 100 cc.
	Blood cholesterol	235 mg. per 100 cc.
	Nonprotein nitrogen	47 mg. per 100 cc.
	Clotting time	2½ minutes
	Bleeding time	3 minutes
	Urine	Negative
	Culture of thoracic fluid	Negative
7/10/44	Red blood cells	4,400,000
	White blood cells	14,000
	Hemoglobin	75 per cent

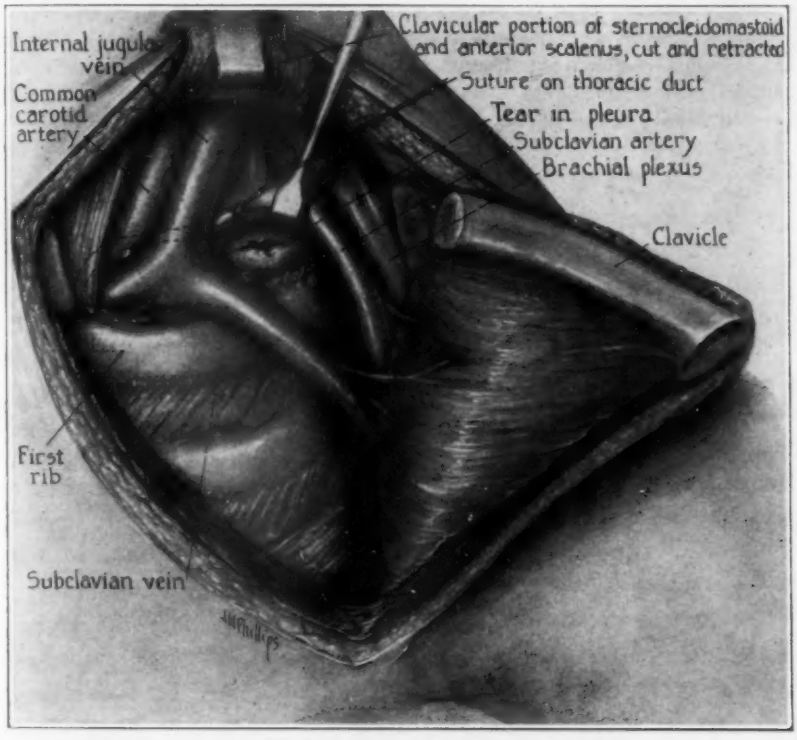
Laboratory Work After Operation

7/11/44	Clotting time	3½ minutes
	Bleeding time	3¾ minutes
One month later	Serum protein	5.6 mg.
	Hematocrit	36 per cent
	Red blood cells	4,490,000
	White blood cells	6,400
	Hemoglobin	14.25 Gm.

His general condition was improved before operation by the administration of 2 units of plasma, 500 cc. of whole blood and 3,000 cc. of 5 per cent dextrose in isotonic solution of sodium chloride.

On July 10, 1944, nine days after admission, with the patient under anesthesia induced by ether administered intratracheally, an incision was made above and parallel to the clavicle. Considerable scar tissue from the trauma from the bullet was encountered. The thoracic duct could not be found, and it was decided to close the hole in the pleura, if this were possible. In order to obtain exposure,

a Sencert [13] type of incision was made. The clavicle was divided with a Gigli saw at the junction of the outer and middle thirds. The incision was swung around the sternoclavicular joint and downward and outward toward the anterior axillary fold. The pectoralis major and minor were detached from the chest, and the tissues swung outward with the outlined flap, after the sternoclavicular joint had been disarticulated. This gave excellent exposure to both the subclavian



Sencert's approach to the first and second portions of the subclavian vessels with the added step of severance of the anterior scalene muscle gave excellent exposure to the apex of the lung and the thoracic duct.

artery and the subclavian vein. After the anterior scalene muscle was divided, the perforation in the apical pleura, 1.5 cm. in diameter, became plainly visible. About 900 cc. of chyle was aspirated from the thoracic cavity, and the hole in the pleura was closed. That the bullet managed to pass between the subclavian artery and vein without damage to either will always remain an act of Providence. A final search for the thoracic duct in the neck revealed some slightly cloudy fluid seeping from behind the internal jugular vein. Elevation of the carotid sheath revealed the severed end, which was ligated with silk.

The following day the patient showed a remarkable change for the better. His former apathy had given way to an alertness that was obvious and a general

13. Bailey, H.: Surgery of Modern Warfare, Baltimore, William Wood & Company, 1941, vol. 1, pp. 299-300.

feeling of well-being. At 10 a.m. sudden dyspnea developed. A roentgenogram taken with a portable apparatus showed a 15 per cent pneumothorax on the right side, and several loculated pockets of fluid were seen on the left. Aspiration of air from the right side of the chest and fluid from the left side controlled his dyspnea, and improvement from then on was continuous. He was discharged to a base hospital on his fifth postoperative day, in good general condition.

A letter received from the subsequent medical officer in charge reported that one month after operation the patient was ambulatory and able to walk 200 yards (183 meters) without dyspnea; his total protein content was now 5.6 Gm. per hundred cubic centimeters; several taps had been necessary to remove small quantities of loculated fluid from the left side of the chest, and he had also recovered from pleurisy on the right side.

DISCUSSION OF THERAPY

It has been aptly shown that ligation of the thoracic duct in the neck can be done with impunity. If the duct is injured during operation, it is important to recognize it and to take the proper simple therapy of suture if the vessel is partially cut or ligature if it is severed. As the wall of the duct is thin and fragile and the pressure mounts considerably after ligation, added security may be obtained by burying the end into muscle or slipping it behind the sheath of a vessel—in the neck, the carotid sheath. Location of the duct may be a serious problem, and it is well to remember that it is most easily found behind the carotid sheath. A suggestion of Shackelford and Fisher, of giving a pint of cream one and one-half hours before operation to which has been added either scarlet red or sudan III, may be helpful.

Chylothorax due to intrathoracic injury offers a more difficult problem, because of the deep situation of the duct. The operative mortality has been reported as 100 per cent, but I have been able to find but 1 case in which ligation in the chest was performed. Whitcomb and Scoville [14] reported a recognized injury to the thoracic duct during a Smithwick operation for hypertension. Both ends of the duct were closed with double silver clips. Dyspnea from chylothorax developed on the seventh day probably due to erosion of the clips on the delicate wall of the duct. Death occurred suddenly, due to an anaphylactic reaction from intravenous administration of chyle. This case demonstrates the necessity of careful protection of the ligatured end of the duct.

In intrathoracic ductal injuries with chylothorax, conservative management has resulted in the appalling death rate of approximately 50 per cent. Conservative therapy consists in thoracentesis to relieve dyspnea, a high protein, low fat diet, intravenous administration of fluids and plasma, administration of amino acids and autogenous trans-

14. Whitcomb, B. B., and Scoville, W. B.: Postoperative Chylothorax, Arch. Surg. **45**:747 (Nov.) 1942.

fusions of chyle. Chyle, when proved sterile by culture, has been given both by direct and by indirect methods, with benefit. Because of the tremendous losses of fluid, dehydration has to be vigorously combated. In patients who recover under conservative management, the rent in the duct is undoubtedly healed over, much as a tear in a ureter.

It would seem logical to pursue conservative therapy for a reasonable period, in the hope of spontaneous closure, but with the patient's condition becoming worse surgical intervention would seem warranted.

The site for intervention is indicated by the side on which the chylothorax was located. In right-sided chylothorax, which predominates, the tear in the duct is usually just above the diaphragm, and a low transthoracic, right-sided approach is indicated. In left-sided chylothorax the tear in the duct is high, and the surgical approach has to be judged accordingly. Brown [15] described a posterior approach for lesions low on the right side, the object of which was to drain the chyle externally. It was undoubtedly hoped that the external fistula would close by contraction.

The difficulties of surgical intervention are appreciated, but they do not appear to be insurmountable and in the failing patient may reduce the extremely high mortality.

CONCLUSIONS AND SUMMARY

1. Chylothorax is a rare condition, 62 cases, including my case, having been reported up to the present time.

2. Injuries of the thoracic duct in the neck, either from accidents or during a surgical operation, are relatively common.

3. The continued loss of chyle results fatally, unless replaced.

4. Ligation of the thoracic duct, at least when injured in the neck, can be done without fear of disastrous results. Collateral circulation is adequate.

5. Chylothorax has had a 50 per cent mortality, and while conservative therapy may be pursued a reasonable length of time operation offers the best hope of reducing this figure.

6. A case of chylothorax, with successful outcome by ligature of the duct in the neck, is reported.

1310 Madison Street.

15. Brown, A. L.: Traumatic Rupture of the Thoracic Duct with Bilateral Chylothorax and Chylous Ascites, Arch. Surg. **34**:120 (Jan.) 1937.

ARTERIOSCLEROSIS OBLITERANS OF THE ABDOMINAL AORTA

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THE NUMBER of patients with slowly progressive thrombosis of the abdominal aorta has been small. In a review of the literature, Greenfield,[1] in 1943, stated that 161 cases of thrombosis and embolism had been reported. In 1940 Leriche [2] presented an excellent summary of the clinical course of progressive thrombosis of the abdominal aorta. On 4 patients he performed a bilateral lumbar sympathectomy, and in 1 patient he excised the lower portion of the abdominal aorta, removed the left lumbar chain and sectioned the right chain below the third lumbar ganglion.

Two patients were recently treated by me, and their cases are being presented in this paper. These cases are to be sharply differentiated from cases of acute embolic obstruction and rapidly progressive thrombosis of the aorta.

The development of the clinical syndrome into a recognizable pattern occurred over the course of three months. In both patients, a collateral circulation adequate to prevent necrosis developed through the upper lumbar, internal mammary and inferior mesenteric arteries. Symptoms appeared in direct relation to the ischemia of the lower extremities and in inverse proportion to the adequacy of the collateral supply. The 2 patients presented similar complaints and physical findings. An extreme fatigability of the lower extremities, intermittent claudication, coldness of the feet, atrophy of the calves and thighs and impotence were found in both men.

Examination revealed cool, pale feet, with few trophic changes in the skin, hair or nails. The pulsations of all major vessels in both lower extremities were absent. Pulsations of the abdominal aorta were easily palpable through the abdominal wall down to the level of the umbilicus but were absent from that point down. Pulsations of the inferior epigastric and circumflex iliac arteries were increased in

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1. Greenfield, I.: Thrombosis and Embolism of the Abdominal Aorta, Ann. Int. Med. **19**:656 (Oct.) 1943.

2. Leriche, R.: Resection of the Iliac-Aortic Bifurcation with Bilateral Lumbar Sympathectomy, in Thrombosis of the Aorta, Presse méd. **48**:601 (July) 1940.

amplitude. The atrophy of the calves and thighs which had been noted by both patients was apparent on examination. The musculature was atonic. Deep reflexes were equal but diminished in intensity. Reflexes in the lower part of the abdomen and cremasteric and plantar reflexes were absent. Whether these alterations represent ischemia of the peripheral nerves or of the spinal cord because of thrombosis of the lumbar arteries is not clearly understood.

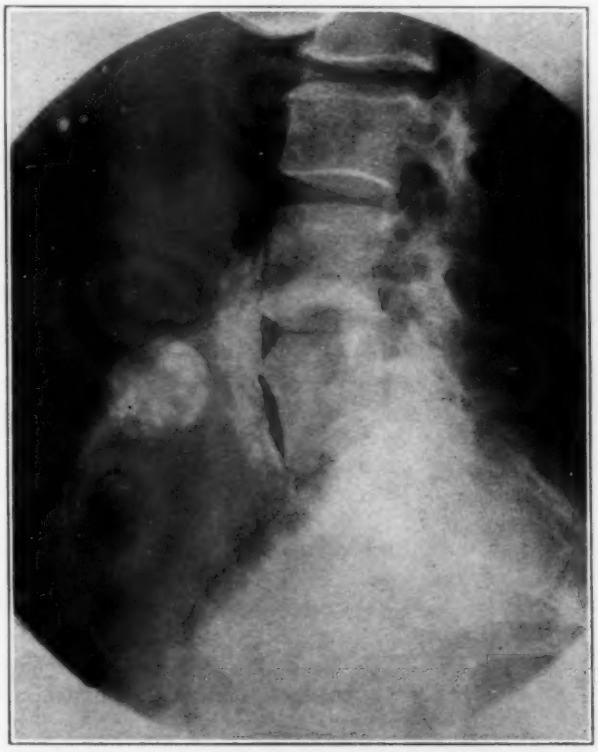

Fig. 1 (case J. C.).—Lateral roentgenogram of the lumbar portion of the spine, showing extensive calcification in the walls of the abdominal aorta and common iliac arteries.

Roentgenographic examination of the abdomen showed in both instances extensive calcification of the aorta in the lower part of the abdomen and the upper portion of both common iliac arteries (fig. 1). Roentgenograms of the extremities showed no calcification in the vessels. Oscillometric readings failed to demonstrate any pulsations in the thighs or calves. Dermathermic readings (fig. 2 A) showed significant elevations in the temperature of the feet following procaine hydrochloride block of the posterior tibial nerve.

Unaware of Leriche's paper at the time these 2 patients were seen, I thought that an interruption of the lumbar sympathetic nerves was indicated to promote as much collateral circulation as possible. This was performed through anterior Pearl [3] incisions. The immediate result was gratifying. Dermathermic readings (fig. 2 *B*) following the left lumbar sympathectomy showed adequate elevation of the temperature of the left foot in both patients. A long enough time has not elapsed to determine the end result of either the disease or the therapy.

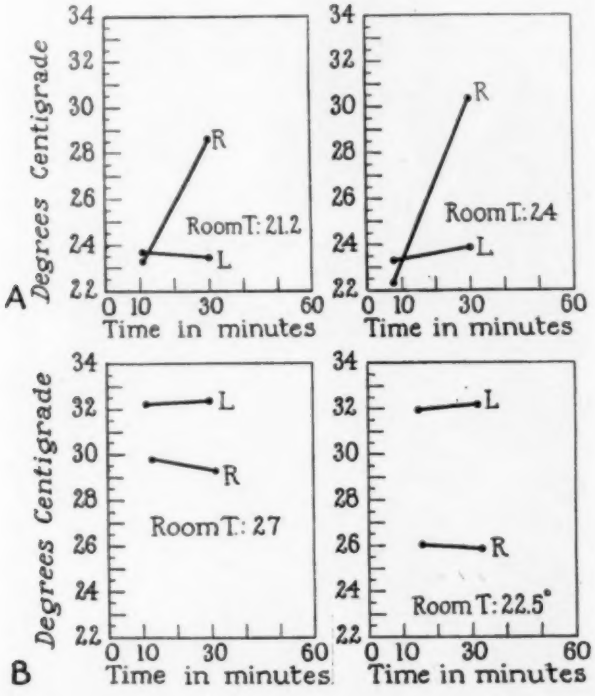

Fig. 2.—*A*, dermathermic readings of the right great toe following procaine hydrochloride block of the right posterior tibial nerve. *B*, dermathermic readings of the left great toe following left lumbar sympathectomy. (Left, case O. M.; right, case J. C.)

REPORT OF CASES

Case 1 (referred by Dr. Harley Williams).—O. M., a 48 year old white man, six months previously had noticed numbness and tingling in the calves and feet after walking up two flights of stairs. During the following few weeks, these sensations arose after he went up short inclines. After he rested three to four seconds, the numbness disappeared. Three months before the admission of the patient to the hospital, the paresthesias were apparent after he had walked two blocks on level ground. At this time, he also observed that his feet felt cold

3. Pearl, F. L.: Muscle-Splitting Extraperitoneal Lumbar Ganglionectomy, Surg., Gynec. & Obst. **65**:107 (July) 1937.

most of the time. During the month prior to admission the tingling had ascended to include the thighs, and at rest a burning pain was present on the lateral aspect of the thighs. He also stated that he had been impotent for several months. There was no disturbance of the upper extremities. The remaining history was irrelevant.

Examination revealed a tall, asthenic, intelligent man. All findings were within normal limits, except those stated in the following paragraphs. Neurologic investigation showed hyperesthesia on the lateral aspect of the left thigh. Deep reflexes were hypoactive, and superficial reflexes were absent. The muscles of the thighs and calves were flabby and atrophic. The pulsations of the aorta were easily palpable down to the level of the umbilicus. No pulsations were present in either lower extremity. The feet were cold and slightly moist to palpation. The color was pale. Venous filling time was twenty-seven seconds on the right and thirty-four seconds on the left.

The urine was straw colored, with a specific gravity of 1.009. There was no albumin or sugar, and the sediment contained an occasional leukocyte per high power field. The hemoglobin was 88 per cent, with a red cell count of 4,700,000. The white cell count was 4,300, with 60 per cent polymorphonuclears, 30 per cent lymphocytes, 8 per cent monocytes, and 2 per cent eosinophils. The serum calcium was 9.8 mg. per hundred cubic centimeters, phosphorus 4.2 mg. per hundred cubic centimeters, alkaline phosphatase 17.3 units, serum cholesterol 308 mg. per hundred cubic centimeters and cholesterol esters 201 mg. per hundred cubic centimeters.

Oscillometric readings showed no pulsations in either calf or thigh. Block of the right posterior tibial nerve with 1 per cent procaine hydrochloride showed a rise in the cutaneous temperature of the foot from 23.3 C. (73.9 F.) to 28.6 C. (83.4 F.). A roentgenogram of the abdomen and legs was reported: "There are linear streaks of calcification in the lower portion of the aorta. The calcification begins with the lower border of the third lumbar vertebra and can be traced as far as the lower border of the fifth lumbar vertebra. There is no other evidence of vascular calcification in the abdomen or legs."

A bilateral retroperitoneal lumbar sympathectomy, which included the excision of the second and third lumbar ganglions, was performed in two stages, without complication. Following the left lumbar sympathectomy, the temperature of the great toe (fig. 2 *B*) measured 32.3 C. (90.1 F.) compared with 29.8 C. (85.6 F.) on the side not operated on. Room temperature was 27 C. (80.6 F.).

One week following the operation, the patient was able to walk for twenty minutes without any pain in the lower extremities. He was readmitted to the hospital two months following the operation, because of a persisting hyperesthesia of the lateral femoral cutaneous nerve on the left side. This was relieved by injections of 1 per cent procaine hydrochloride into the lateral femoral cutaneous nerve and short wave diathermy to the lumbar area. He had had satisfactory sexual relations since discharge from the hospital.

Case 2 (referred by Dr. Elton Recroft).—In J. C., a 46 year old white man, increasing intermittent claudication of both calves had developed six months previously. More pain was felt in the left than in the right calf. He observed that the left foot was colder than the right. Symptoms were more prominent in cold, wet weather. He had been impotent for several months. The patient had been receiving a deproteinated pancreatic extract, which had increased his tolerance to exercise more than twofold. The past history revealed a fall on his back one

year prior to admission. This disabled him for only a few days. Five years ago, he was told that he had a calcium deficiency and was given 8 calcium tablets each day for three to four months. The dosage was not known. The remaining history was noncontributory.

Physical examination showed a well developed, well nourished, intelligent man appearing older than his stated age. The remainder of the examination showed no abnormalities except in the peripheral vascular and peripheral nervous systems. No pulsations of the aorta were present below the umbilicus, and no pulsations were palpable in any of the arteries of the lower extremities. Both feet were slightly cool. Venous filling time in the feet was thirty-five seconds and forty-two seconds on the right and left respectively. Deep reflexes in the lower extremities were hypoactive, and the musculature was atrophic.

The urine was clear, with a specific gravity of 1.001. There was no albumin or sugar, and the sediment contained 2 to 4 white blood cells per high power field. The hemoglobin was 110 per cent and the white cell count 7,150. The serum calcium was 10.7 mg. per hundred cubic centimeters, phosphorus 3.7 mg. per hundred cubic centimeters, alkaline phosphatase 5.2 units, serum cholesterol 207 mg. per hundred cubic centimeters and cholesterol esters 90 mg. per hundred cubic centimeters.

Oscillometric readings showed absence of pulsations in both lower extremities from the groin to the periphery. Following a posterior tibial block on the right with 1 per cent procaine hydrochloride, the temperature (fig. 2 *A*) of the great toe rose from 22.4 C. (72.3 F.) to 30.4 C. (86.7 F.), while the control remained at 23.9 C. (75.1 F.). The electrocardiogram was normal. Roentgenologic examination (fig. 1) showed severe calcific sclerosis of the abdominal aorta in front of the fourth and fifth lumbar vertebrae. There was no calcification in the vessels of the legs or feet.

A bilateral retroperitoneal sympathectomy was performed in two stages according to Pearl's technic. During the course of the left lumbar sympathectomy, the aorta was exposed. Pulsations were good down to 2 to 3 cm. above the bifurcation. Below this point, the aorta was about two-thirds its normal size, thickened and pulseless. The left common iliac artery also had no pulsations in the exposed 3 to 4 cm. The procedures were uncomplicated. The resting temperature of the great toes (fig. 2 *B*) rose to 32.1 C. (89.7 F.), and the extremities showed no sudomotor activity. Two months following the operation the patient's only complaint was mild aching in the thighs on arising in the morning. This disappeared during the day.

SUMMARY

Two cases of arteriosclerotic calcification and thrombosis of the abdominal aorta have been presented. The thrombosis occurred in men of 46 and 48 years. The relation of the autonomic nervous system to the collateral circulation and its interruption as a means of increasing that circulation is mentioned.

The incidence of this disease is probably much higher than is generally appreciated. The appearance of the extremities does not at first suggest arterial deficiency. The complaints referable to both lower extremities should lead to a careful examination of the peripheral pulses

and abdominal aorta. The interpretation of the neurologic changes is difficult and will have to await microscopic examination of the spinal arteries, spinal cord and peripheral nerves. Oscillometric determinations and roentgenographic examination of the abdomen are helpful. The advisability of resecting the abdominal aorta as Leriche [2] reported should be considered in each individual patient. In general, however, to subject a patient to this procedure seems unwarranted, since the reaction itself should theoretically accomplish little in promoting collateral supply to the lower extremities.

ACUTE FULMINATING ULCERATIVE COLITIS WITH MASSIVE PERFORATION AND PERITONITIS

Report of a Case

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THE RECENT opportunity to study in the ward and in the pathology laboratory a case of acute fulminating ulcerative colitis with massive perforation and peritonitis stimulated a review of the literature in this regard. Its rarity together with its urgent therapeutic demands prompts me to present the following study of a case with a review of the literature.

REPORT OF A CASE

T. H. was a 43 year old, white woman, a divorcee, who was brought to the hospital in a state of profound shock. Her chief complaint was diarrhea of four weeks' duration. Because of her persistently critical condition and the absence of relatives, the history obtained is lacking in detail and probably to some extent in accuracy.

She was born in Oregon, had lived in the United States all her life and had come to Boston a few months previously. She had been married and divorced, was childless and had been employed as a millinery shop worker. Her health in the past had been good with a single exception. In California two years previously she had been hospitalized with postpneumonic empyema on the left side, drained by rib resection with subsequent thoracoplasty. Absolutely no significant history could be obtained of previous gastrointestinal disturbance, recent known exposure to enteric infection or food poisoning. There was no history of tuberculosis or contacts with tuberculosis.

Present Illness.—The immediate illness probably began about six weeks before entry, with stiffness and soreness of the muscles of the extremities and shoulder girdle. These symptoms were accompanied with slight malaise. There was no history of the patient's having ingested inadequately cooked pork or having had fever, alterations in bowel habits or abdominal cramps. She had felt well within a few days.

Four weeks prior to entry there was the insidious onset of moderately severe, crampy pain throughout the abdomen. Bowel movements occurred three times daily instead of once and afforded no relief from the abdominal distress. Stools were usually light yellow but occasionally black and always loose in consistency. The patient had never observed red blood in her stools prior to her entry into the hospital. Accompanying her diarrhea, anorexia began, which later became

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increasingly severe. There was no nausea, vomiting or localized pain. Three weeks before admission a low grade fever started. Abdominal pain became severer and was more pronounced on the left side. By ten days before entry, diarrhea, pain and weakness reached severe proportions and, in addition, the patient was persistently drowsy. During a single visit to her home, a local physician made a diagnosis of "intestinal influenza"; no chemotherapy or specific treatment was instituted. A Christian Science practitioner subsequently cared for the patient until her entry to the hospital. On the day of admission, she remembered only that the diarrhea was distinctly worse, with nearly continuous, watery, brownish yellow movements and generalized abdominal pains.

Physical Examination on Entry.—The temperature was 97.8 F., the pulse rate 120, the respiratory rate 36 and the blood pressure 85 systolic and 70 diastolic. She was critically ill, a fairly well preserved middle-aged woman in profound collapse. She seemed oriented but drowsy. She had no spontaneous pain. The extremities were cold, with a barely perceptible pulse at the wrist. The cheeks were sunken, but only slight generalized loss of weight was evident. The skin and mucous membranes were dry and generally pale, save for distinct reddening of the thenar and hypothenar eminences. No eruptions, petechiae or telangiectasia were observed. There was no local or general enlargement of the lymph nodes. The finger tips showed mild clubbing. The tongue was dry but not atrophic. The respiratory excursion was regular, rapid and shallow. In the lungs no abnormalities by percussion or auscultation were noted except for evidence of a thickened pleura at the left base, about the site of the old scar for empyema drainage. The heart seemed normal in size. The sounds were faint, and no murmurs could be detected. The peripheral veins were not visible, and on attempting to cut into the saphenous vein to give fluids we found that it was collapsed. The abdomen was distended, fairly tense and tympanitic. No mass or peristalsis was visible. There were diffuse generalized rebound and percussion tenderness and pain everywhere on pressure. No organs or masses were felt. No peristaltic sounds were audible. There was no evidence of a fluid wave. Pelvic examination revealed a rectovaginal fistula just inside the introitus, close to the posterior fourchet. There was moderate tenderness in the vaults, but no masses were felt. The rectal examination gave rise to considerable pain on pressure in all directions. No masses were noted. The neurologic findings were within normal limits.

Laboratory Data.—The hemoglobin content on entry was 7.8 Gm. It rose after repeated transfusions during the next three days to 12.2 Gm. The red cell count ranged from 2,900,000, on entry, to 4,280,000 after transfusion. The white blood cell counts ranged from 28,000, on admission, to 16,000, three days later. On smear there were many juvenile polymorphonuclear leukocytes, with a total count ranging from 92 to 95 per cent. No abnormal cells were seen.

Routine specimens of the urine concentrated to 1.022. No protein or sugar was present. Acetone was noted on entry, but none was subsequently found. Occasional red blood cells, white blood cells and hyaline casts were found in centrifuged sediment analyses.

The first stool examined after admission was brownish yellow and semiliquid and contained no blood according to the guaiac test. Subsequently, many stools were grossly bloody, with both bright red and changed blood. Smears of fecal material were negative for Endamoeba histolytica, Balantidium coli and Mycobacterium tuberculosis. Stool cultures were negative for pathogens; Bacillus morgani was obtained, but this did not agglutinate in anti-Shiga or in polyvalent antidysentery serums.

During life, blood was difficult to obtain and serologic tests of the blood, agglutination tests and culture studies were never done. Determinations of blood chemistry on heart blood immediately following death showed blood urea nitrogen 45 mg. per hundred cubic centimeters, nonprotein nitrogen 110 mg., total protein 6.5 Gm., albumin 3.6 Gm. and globulin 2.9 Gm.

Hospital Course.—After entry the patient's temperature fluctuated irregularly from 98.8 to 101.2 F. The pulse was always rapid, with an average reading around 115. Shortly after admission, the patient received 500 cc. of plasma, 1,000 cc. of compatible, cross-matched blood and 3,000 cc. of solutions containing sugar and isotonic solution of sodium chloride given intravenously. This resulted in considerable general improvement. Her blood pressure rose to 115 systolic and 75 diastolic, and concomittantly her heart sounds became readily audible, with a grade II precordial systolic murmur. A roentgenogram of the chest showed only an elevated left diaphragm and a thickened pleura on that side, close to the site of the old rib resection. The heart and lungs appeared normal. Abdominal roentgenograms demonstrated moderate distention of the entire colon and blurring of the peritoneal lines. A roentgenogram of the abdomen with the patient in the erect position on the second day in the hospital showed no free air under the diaphragm.

Daily treatments included repeated attempts to pass a Miller-Abbott tube to relieve distention and the administration of plasma, blood and solutions containing salt and sugar.[1] Sodium sulfadiazine was given parenterally. Improvement continued for three days, with a slight drop in the pulse rate, stabilization of the blood pressure, clearing of the mental state and decrease in discomfort. There was no nausea or vomiting. The abdomen, however, remained unchanged, with distention, tenderness and absence of peristalsis. On the fourth hospital day the patient began to pass large amounts of bright red blood by rectum. Her blood pressure fell. She went into profound peripheral collapse, which was not remedied by repeated transfusions.[1] Rectal hemorrhage continued, and the patient died on the morning of the fifth day in the hospital.

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1. Fluids administered were as follows:

10/20/43	Whole blood, 1,000 cc. given intravenously	
	Plasma, 250 cc. given intravenously	
	Plasma, 250 cc. given intrasternally	
	5 per cent dextrose in isotonic solution of sodium chloride, 2,000 cc. given intravenously	
	5 per cent dextrose in water, 1,000 cc. given intravenously	
	5 per cent dextrose in water, 1,000 cc. given by clysis	
	Total	5,500 cc.
10/21/43	5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously	
	5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intrasternally	
	5 per cent dextrose in water, 1,000 cc. given intrasternally	
	Total	3,000 cc.
10/22/43	5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously	
	5 per cent dextrose in water, 1,000 cc. given intravenously	
	Plasma, 250 cc. given intravenously	
	Total	2,250 cc.
10/23/43	Whole blood, 1,000 cc. given intravenously	
	Plasma, 500 cc. given intravenously	
	5 per cent dextrose in water, 1,000 cc. given intravenously	
	5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given by clysis	
	Total	3,500 cc.
10/24/43	Plasma, 250 cc. given intravenously	
	5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously	
	5 per cent dextrose in water, 1,000 cc. given by clysis	
	Total	2,250 cc.

Autopsy Report.—On Oct. 25, 1943, ten hours after death, a complete necropsy was performed.

Gross Pathology.—Body: The body was well developed and well nourished, with an abundant amount of subcutaneous fat of normal distribution. The skin was ashen gray, finely textured and moderately dehydrated. The left side of the chest had a well healed, slightly depressed gray scar 10 cm. in length. On this side the thoracic wall was depressed and devoid of a normal bony cage over an area measuring 15 by 8 cm. Parts of the third, fourth, fifth and sixth ribs had been removed for local thoracoplasty after the patient's empyema was drained. Each rib lacked about 9 cm. of its total length.

The hair was finely textured, dark brown and of normal distribution. The eyeballs were unusually soft. The mucous membranes of the turbinates were crusted with dark brown material. The lips were dry, cracked and cyanotic.

The abdomen was ballooned out considerably, giving the appearance of an immense dome, whose apex was just below the navel. There were no dilated veins. The umbilicus was shallower and broader than usual. There was a fluid wave detectable in the flanks. The midabdomen anteriorly was tympanitic. The liver and spleen were not palpable. No other masses were made out, and no hernias were found.

The external genitalia were normally developed. Skene's and Bartholin's glands were not enlarged. The introitus admitted three fingers. The cervix was flat, firm and free of erosions. The perianal skin was excoriated. The mucocutaneous junction was prolapsed, 5 to 7 cm. being entirely visible. The rectal examination showed a small rectovaginal fistula, 2.5 cm. in diameter, 2 cm. inside the anal sphincter.

Peritoneal Cavity: When the abdominal cavity was opened, a large amount of gas escaped. Subsequently 2,100 cc. of chocolate brown, soupy fluid with a fecal odor was removed. This contained many free floating tabs of partially necrotized fatty tissue together with numerous droplets of liquid fat. The central portion of the omentum had several rents, where fat and its peritoneal covering had disappeared, leaving a skeleton of the larger vessels (fig. 1). Its right wing was attached to the anterior parietal peritoneum in the right lower quadrant; its left wing was attached to the upper sigmoid at the brim of the pelvis. Loculated, fecal-stained fluid was present in practically all recesses of the abdomen; 250 cc. was moved from the suprahepatic area, 250 cc. from the pelvis and 250 cc. from under the dome of the left diaphragm. Only the lesser peritoneal cavity was free of contamination; the foramen of Winslow was sealed off with fibrinous exudate.

The most striking feature was found in the large intestine. From the ileocecal valve to the rectosigmoid junction at the brim of the pelvis,

there was a continuous defect, involving all coats of the ventral (antimesenteric) side of the colon (fig. 1). The posterior half of the large intestine remained as an open trough in direct communication with the peritoneal cavity. This mucosa in some areas had been completely ulcerated away; in other areas irregular mucosal strands remained. The ulcerative process had burrowed deep into the submucosa, undermining cobweb-like shreds of mucosa. The result was a lacelike pattern covered with yellow fibrin on an irregularly burrowed and ulcerated submucosa and muscularis. No hemorrhages were noted. The entire large bowel

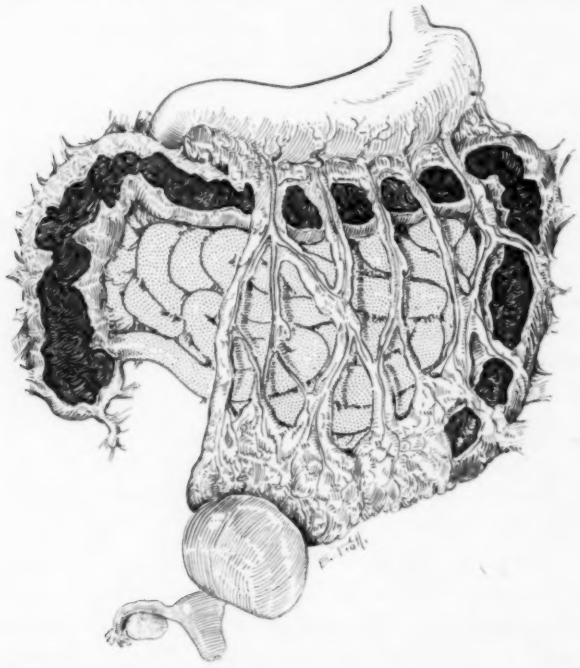

Fig. 1.—Diagrammatic illustration of massive ulceration of entire colon with destruction of antimesenteric border, with fenestration of the omental apron and with a large hydrosalpinx on the left side.

had previously been considerably dilated, because there was a pressure imprint on the inner surface of the anterior wall of the peritoneum.

In general the viscera were normal in size, shape and position. The liver was enlarged and extended down 6 cm. below the right costal margin in the midclavicular line. Its external surface was dark greenish brown, with some fibrin deposited on its peritoneal covering. The spleen was unusually small and flabby. The stomach had a hyperemic serosa with fibrinous exudate.

The small intestines were matted together with fibrinous exudate. Portions of the external surface of the small intestines which had come

into contact with the exposed posterior mucosa of the large intestines were eroded through the serosa and into the muscularis.

The pancreas was short but of usual breadth and depth. It was entirely enclosed in peripancreatic fat, the anterior portions of which appeared autolysed. The kidneys were not remarkable. In the pelvis the bladder was partially distended. The uterus was covered with fibrin.

To the right broad ligament was attached a small ovarian mass which was dark green, cystic, well encapsulated and 4.5 cm. in diameter. The left broad ligament was involved in an old inflammatory process involving the left tube, ovary, sigmoid and lateral uterine wall. The epiploic appendixes were adherent to the left tubo-ovarian inflammatory mass by dense fibrous adhesions.

Pleural Cavities: The right pleural cavity was normal except for a few fibrous adhesions on the posterior wall of the middle lobe. The left pleural cavity was obliterated by thick, dense, fibrous adhesions. These were most pronounced in the region of the rib resection and thoracoplasty. The anterior and superior aspects of both lungs were mottled pink and gray; the inferior and posterior surfaces were dark red and firm.

Heart: The heart weighed 300 Gm. This organ was essentially normal except for a shaggy, hard, wafer-shaped nodule about 4 mm. in diameter on one of the mitral cusps along the line of closure. There was no fresh friable thrombus. There was a firm annulus fibrosis. The myocardium and coronary vessels were not unusual.

The Lungs: The right lung weighed 420 Gm. and the left 280 Gm. Aside from the pleural adhesions already described, the only abnormality was an old, healed tuberculous nodule in the parenchyma of the left apex. The dark and firm character of the posterior and inferior aspects of both lungs was consistent with venous stasis. No pulmonary thrombi were found.

Alimentary Tract: The esophagus was normal. The stomach, duodenum, jejunum and ileum displayed fibrinous adhesions externally with irregular and scattered areas of serosal erosion previously mentioned. The mucosa was congested but free of hemorrhages, ulcerations and perforations.

After several days in 10 per cent solution of formaldehyde the sigmoid and rectum were opened. The same burrowing, necrotizing phlegmonous process was identified down to the mucocutaneous junction. No area of the large bowel was entirely free of the ulcerative process, although the midsigmoid was least affected. The ileocecal valve was opened from the proximal side. All the mucosa on the cecal side was involved in the inflammatory process, but the ileum was unaffected.

At the time of the gross autopsy the aorta was opened as well as the celiac axis, superior mesenteric artery and inferior mesenteric artery to their first bifurcations. No thrombi were observed. After fixation in solution of formaldehyde, dissection of these vessels to their attachments to the intestines was completed and no thrombi were observed.

Pelvic Organs: The bladder and uterus were not abnormal. The cystic tubo-ovarian mass on the right side was full of thick chocolate brown fluid. After fixation in 10 per cent solution of formaldehyde, the mass in the left broad ligament involving the sigmoid, uterus, ovary and tube was dissected. Another old scarred, walled-off, tubo-ovarian abscess was encountered, full of material similar to the one on the opposite side.

Brain: The weight of the brain was 1,340 Gm. There was no cerebral edema. No foci of hemorrhages, necrosis or thrombosis were found. After fixation in solution of formaldehyde, the brain was sectioned and the region of the thalamus and hypothalamus particularly carefully examined. No unusual observations were made.

Spleen, Liver and Kidneys: The spleen, liver and kidneys were not unusual.

Microscopic Pathology.—Heart: The suspected vegetation on the mitral valve showed only a local collection of hyaline material of fairly recent deposition. Otherwise the myocardium, endocardium and epicardium were not remarkable.

Lungs: Some congestion and patches of emphysema were the only abnormal findings.

Pancreas: No evidence of pancreatitis was found. There were patches of fibrosis and hyalinization at the expense of acinar tissue.

Stomach and Small Intestine: In several sections the serosa was involved in an acute inflammatory process, which occasionally extended into the outermost portions of the muscularis. The vessels were congested. The lymphatics were dilated. Large monocytes, plasma cells and large numbers of polymorphonuclear leukocytes had infiltrated the inflamed serosa. The mesothelial covering was discontinuous. The lining mucosa and submucosa were not abnormal.

Large Intestine: In all sections, observations corroborated the gross picture. In most areas the mucosa was completely ulcerated away (fig. 2). Where present, the muscularis mucosae was increased in prominence and thickness. Plasma cells and polymorphonuclear leukocytes had infiltrated all layers. A thick acidophilic membrane of fibrin and debris covered the ulcerated surfaces. The necrotizing process had extended into the submucosa and muscularis in many areas (fig. 3). Strands of coagulated fibrin separated submucosal hyaline connective tissue.

Lymphatics were dilated and full of granular debris. Blood vessels were surrounded by leukocytes; yet no evidence of a necrotizing arteriolitis was observed. In some zones even the muscularis had been destroyed. No inclusion bodies were observed. No amebas, trichinas, Balantidia or other parasites were found.

Spleen: The spleen displayed a mildly congested red pulp with scattered collections of polymorphonuclear leukocytes.

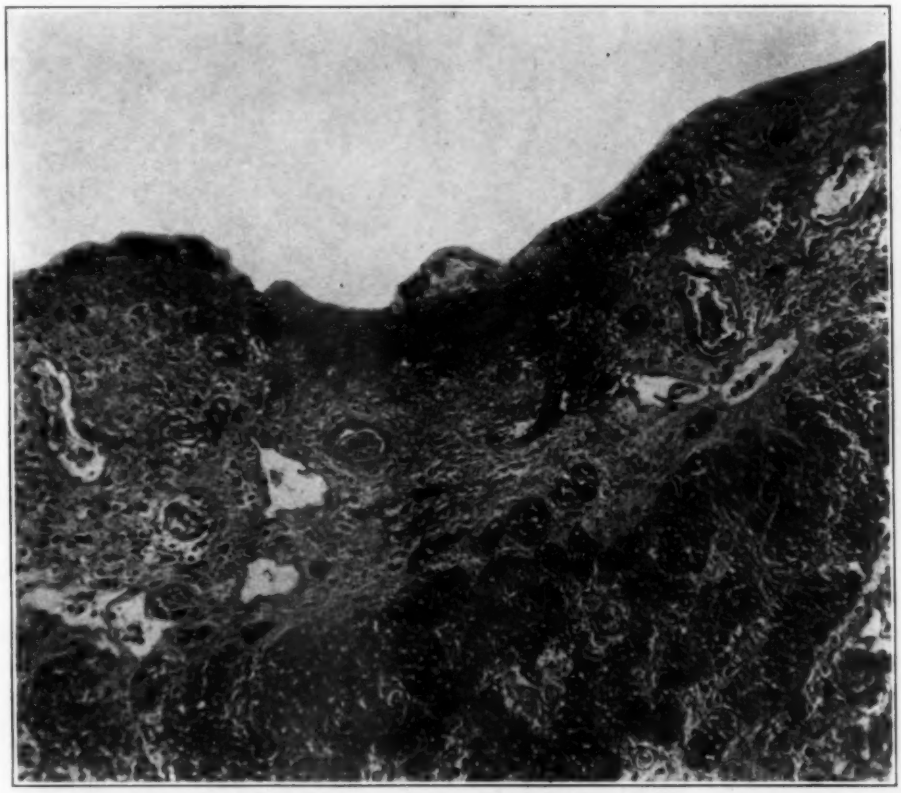

Fig. 2.—Microscopic view (× 50) of the rectal mucosa, showing the absence of the mucosa, erosion into the submucosa, congested vessels and dilated lymph vessels.

Liver: The liver was not abnormal.

Kidneys: In the kidneys, a few glomerular tufts contained fibrin thrombi but no congestion, inflammation or arteriolitis was observed. The tubules and renal pelves were not unusual.

Postmortem Bacteriology.—Cultures of the heart blood yielded Bacillus coli, Staphylococcus aureus and Staphylococcus albus. Cultures

of the peritoneal fluid yielded B. coli, Clostridium alcaligenes, Staph. aureus, Staph. albus and an alpha hemolytic streptococcus. Staph. aureus colonies were coagulase negative. Swabs taken from the rectal mucosa and cultured according to Bargen's technic failed to yield diplostreptococci.

Summary of the Postmortem Findings.—The body showed acute ulcerative colitis with extensive necrosis resulting in the disappearance

Fig. 3.—Microscopic view (× 60) of the cecal mucosa, showing discontinuity of the mucosa, erosion into the submucosa, congested vessels and dilated lymph vessels.

of the ventral (antimesenteric) half of the entire colon, from the ileocecal valve to the sigmoid. The remaining wall of the large bowel appeared as an open trough with severe cellulitis and erosion into the submucosa and muscularis. Accompanying this massive dissolution of the bowel wall was fecal peritonitis with 2,100 cc. of loculated purulent fluid. Anal excoriations and a rectovaginal fistula were noted. Incidental findings included a recent mitral valvular vegetation, old bilateral fibrous pleuritis, bilateral tubo-ovarian abscesses and atrophy of the pancreas.

REVIEW OF THE LITERATURE

Most publications on ulcerative colitis are concerned with the chronic forms. In 1942, Brown, Buie and Weber [2] published an excellent classification of these conditions, largely based on endoscopic examinations. In 1943, Bargen [3] published a monograph on "The Modern Management of Colitis," in which he classified colitis into nine separate groups; his is probably the best known and generally accepted classification. Under colitis he lists type I, tuberculous ulcerative colitis, caused by Myco. tuberculosis; type II, amebic ulcerative colitis, caused by E. histolytica; type III, bacillary dysentery, largely caused by several forms of organisms of the Shigella paradysenteriae group; type IV, thromboulcerative colitis, caused by the Diplostreptococcus [4]; type V, ulcerative colitis, caused by the virus of lymphogranuloma venereum; type VI, allergic colitis; type VII, colitis as part of the syndrome of dietary deficiencies; type VIII, chronic ulcerative colitis of unknown origin but definitely not caused by the Diplostreptococcus, and type IX, segmental ulcerative colitis, of unknown etiology. The last differs from type VIII only in distribution.

In all these conditions chronicity is outstanding except in a small group of cases under the classification of thromboulcerative colitis. Cases under this general classification Bargen described as being "insidious," "severe" or "fulminating" in onset. Of 871 cases of thromboulcerative colitis which he studied at the Mayo Clinic, there were 163 cases of "fulminating" colitis; only 21 of these ended fatally. Little pathologic information is available concerning this group of patients. In a previous paper, in 1940, Schlicke and Bargen [5] reported 20 cases of "fulminating" ulcerative colitis; in these only 3 patients had had symptoms of less than one year's duration. Nearly all exhibited an intermittent course, with chronicity as a prominent feature; acute ulcerations with perforations were merely terminal events. In all these reports it seems clear that these authors were dealing essentially with chronic colitis, a condition unlike that in the case under discussion. Furthermore, the Diplostreptococcus was recovered in 19 of the 20 cases of "fulminating" colitis reported by Schlicke and Bargen but not in the present case.

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2. Brown, P. W.; Buie, L. A., and Weber, H. M.: An Unclassified Type of Ulcerative Disease of the Colon, South. M. J. **35**:305, 1942.

3. Bargen, J. A.: The Modern Management of Colitis, Springfield, Ill., Charles C Thomas, Publisher, 1943, p. 322.

4. The Diplostreptococcus is more commonly referred to in this condition as Bargen's bacillus.

5. Schlicke, C. P., and Bargen, J. A.: Fulminating Ulcerative Colitis: A Critical Analysis of Twenty Cases, Minnesota Med. **23**:348, 1940.

Since 1933 there have been 4 separate instances of simple acute ulcerative colitis among the Cabot case reports in the *New England Journal of Medicine*.[6] All the cases were without antecedent history of gastrointestinal disturbance, ran acute courses of less than nine weeks' duration and ended fatally, with perforation of the ulcerated colon and peritonitis. In 1937, Bunch [7] reported another acute case of phlegmonous ulcerative colitis with perforation and peritonitis; his patient died in a few days. In the discussion of Cabot Case 19,021,[6a] the late Dr. Daniel Jones stated that he had seen 2 or 3 similar patients, a few of which had recovered. He contended, together with Dr. Chester Jones, that this was a different entity from chronic ulcerative colitis with an acute "fulminating" terminal phase. Dr. Charles Lund [6a] is accredited with having saved a woman with a similar condition by doing an ileostomy and cutting the anal sphincter away from the infected colon for maximum drainage. The table summarizes the salient features of these 5 cases together with the present one.

From the table it is clear that in this group of cases age and sex are of no significance. All patients had diarrhea, some bloody, and others puriform and some with pain and 1 with no pain. The total duration of illness ranged from two days, in case 3, to nine weeks, in case 4. All had acute fulminating courses, with generalized peritonitis following perforation of the ulcerated colon. Five had a definite ulcerative process from the cecum to the rectum, and in only 1 was the process primarily confined to the descending colon. Five of the 6 patients were submitted to operation. Carefully selected surgical intervention in the case reported in this article might well have altered for the better the fatal course of the patient.

Although the laboratory studies are not complete in all 6 cases, it can be safely stated after a careful review of the available data that no known etiologic mechanism is detectable. Bargen was able to recover the Diplostreptococcus in most of his cases of acute "fulminating" ulcerative colitis. In at least 2 of these 6 cases this organism was sought but not recovered, despite the use of the technic recommended by

6. (*a*) Acute Ulcerative Colitis with Perforation, Cabot Case 19021, New Eng. J. Med. **208**:89, 1933; (*b*) Acute Idiopathic Colitis with Perforation of Transverse Colon, Cabot Case 23201, ibid. **216**:894, 1937; (*c*) Ulcerative Colitis with Perforation of Cecum, Cabot Case 24041, ibid. **218**:183, 1938; (*d*) Acute Idiopathic Ulceration Colitis with Perforation, Cabot Case 27242, ibid. **224**:1029, 1941.

7. Bunch, G. H.: Acute Phlegmonous and Non-Traumatic Perforative Lesions of the Colon: Report of Three Cases with Intraperitoneal Hemorrhage Complicating One, South. Surgeon **6**:449, 1937.

Salient Features of Five Cases From the Literature and Present Case

Case	Total Duration of Disease	Sex	Age, Yr.	Chief Complaint	Operation	Comment	Pathologic Findings at Examination
1. Cabot case 19021 (1933).....	6 weeks	F	22	Diarrhea for 4 wk.	Exploratory laparotomy; ileostomy	Diffuse peritonitis found at operation; died 18 hours after operation	Ulceration of entire colon; perforation of sigmoid; generalized peritonitis
2. Bunch (1937).....	3 days	M	35	Abdominal pain and nausea for 48 hr.	Exploratory laparotomy; suturing of perforation	Several inches of colon necrotic and perforated at operation; hemorrhaging from perforation; died 25 hours after operation	Gangrene of descending colon; perforation; hemorrhage and peritonitis
3. Cabot case 23201 (1937).....	2 days	M	60	Abdominal pain for 1 day	Exploratory laparotomy	Diffuse phlegman of colon found at operation	Ulceration of entire colon; multiple perforations; generalized peritonitis
4. Cabot case 24041 (1938).....	9 weeks	F	56	Ischiorectal abscess for 3 weeks.	1. Incision and drainage of ischiorectal abscess; 2. Exploratory laparotomy drainage of abscess; Witzel enterostomy	Patient became distended and vomited after incision and drainage of abscess; abscess in right lower quadrant drained of laparotomy and ileostomy; died 3 days later	Ulceration of entire colon; perforation of cecum with abscess; generalized peritonitis
5. Cabot case 27242 (1941).....	8 weeks	F	39	Bloody stools for 7 weeks.	Cecostomy and appendicostomy	Had had hemorrhoidectomy 2 weeks before entering Massachusetts General Hospital; died 3 days after cecostomy	Ulceration of entire colon; perforation of sigmoid; generalized peritonitis
6. Present case (1945).....	5 weeks	F	43	Diarrhea for 4 wk.	None	Patient improved for first 3 days in hospital; began hemorrhaging on 4th day; died on 5th day	Ulceration of entire colon; perforation of colon from cecum to sigmoid; generalized peritonitis

Bargen in 1935.[8] Mones and Sanjuan[9] expressed the opinion that a virus accompanying Bargen's diplostreptococcus was the causative agent in thromboulcerative colitis. In the study of the postmortem material in this case, inclusion bodies were carefully looked for but none were observed.

In 1940, Schlicke and Bargen[10] called attention to the fact that clubbed fingers occur oftener in conjunction with chronic ulcerative colitis than is generally appreciated. It is of interest to note that the case reported in this article is the only 1 of the 6 reviewed cases in which this condition was found. Whether this is an end result of the prolonged experience with pneumonia, empyema and thoracoplasty or with an unsuspected colonic lesion of long standing is a matter for conjecture.

CLINICAL COMMENT

The clinical diagnosis in cases of acute fulminating ulcerative colitis is probably best reached by exclusion. Tuberculous ulcerative colitis usually runs a chronic course, is oftener seated in the ileocecal region first and, by the time it involves the rectum, is frequently accompanied with multiple fistulas and sinuses. Pulmonary tuberculosis is commonly an accompaniment of tuberculous ulcerative colitis. Proctoscopic examination reveals irregularly shaped, shallow ulcers with yellow caseous bases often covered with a gray pellicle of fibrin. Recovery of Myco. tuberculosis from the stool is pathognomonic. Amebic dysentery is sometimes acute but oftener chronic in nature. On proctoscopic examination the ulcers are punched out and sharply delineated, with slightly elevated margins and grayish white fibrin caps over the bases. Identification of E. histolytica in stool preparations is diagnostic. Lymphogranuloma venereum occasionally runs a fulminating course with acute diarrhea. This occurs most frequently in Negroes. The Frei test is nearly always positive, although some patients acutely ill with lymphogranuloma have had repeatedly negative Frei tests until they began to improve. Bacillary dysentery due to Bacillus typhosus, Bacillus paratyphosus, B. coli and Shigella dysenteriae may run a severe fulminating course. Proctoscopic examination reveals no zone of the mucosa which is free of inflammation. The angry redness of pronounced hyperemia is striking. Petechial hemorrhages, shallow irregular ulcers

8. Bargen, J. A.: The Management of Colitis, edited by M. Fishbein, National Medical Monograph, New York, National Medical Book Company, Inc., Doubleday, Doran & Company, Inc., 1935, p. 233.

9. Mones, F. G., and Sanjuan, P. D.: Grave Ulcerative Colitis Without Amebic Etiology: Diagnosis with Lucid Treatment, Am. J. Digest. Dis. & Nutrition **4**:247, 1937.

10. Schlicke, C. P., and Bargen, J. A.: "Clubbed Fingers" and Ulcerative Colitis, Am. J. Digest. Dis. **7**:17, 1940.

with angry red bases, edematous intervening mucosa—all contribute in making the diagnosis by direct visualization. Appropriate pathogenic organisms can be recovered by differential cultural methods. If the patients run a long enough clinical course, results of agglutination tests of the blood often become positive. Colitis due to Ballantidium coli may occur with acute diarrhea in any part of the world where hog meat is in the diet. Recovery of the large infusorian organisms from the stools is diagnostic. Diverticula of the large bowel with colitis are not uncommon. In this condition the illness usually occurs in an older age group and is customarily accompanied with premonitory signs and symptoms of rumbling abdominal cramps, intermittent bouts of diarrhea and localized abdominal tenderness. Later, chills and fever accompany severer diarrhea. These cases sometimes go on to intestinal obstruction when a palpable tender mass with local spasm is detectable. Carcinoma of the large intestine with ulceration, bleeding and diarrhea is also usually limited to an older age group and is accompanied with loss of weight and change in bowel habits running over a much longer period. Thromboulcerative colitis with severe diarrhea, variously termed idiopathic ulcerative colitis, colitis gravis and nonspecific ulcerative colitis, has an easily distinguishable proctoscopic picture which is fairly diagnostic. The mucosal lining is glazed, and over it are scattered multiple tiny gray granular dots, of less than a millimeter in diameter. When the mucosa is touched with an instrument, bleeding occurs readily. The lumen is narrowed, and the wall is diminished in flexibility. Tiny pocket-like scars are occasionally seen in cases of longer standing. This is the group of patients from whom Bargen has been able to culture the diagnostic Diplostreptococcus.

The 6 cases of acute fulminating ulcerative colitis listed in table 1 do not correspond to any of Bargen's types. In none is there a history of recent consumption of improperly cooked pork, exposure to tuberculosis or change in bowel habits. In only 1 instance was there a family history of ulcerative colitis; in that patient, whose brother had had the disease, there was history of loss of weight, overwork and emotional stress during the preceding year. In 1 other case the patient had vague rumbling left-sided abdominal cramps for several months before the onset of the immediate illness. The patients in the remaining 4 cases had explosive onsets of their intestinal disturbances. Unfortunately, because of the short duration and gravity of their illnesses, no proctoscopic findings were available.

Treatment of these patients was first supportive. They were given intravenous injections of dextrose and isotonic solution of sodium chloride, infusions of whole blood and plasma, sulfonamide drugs and chiniofon. To this armamentarium, penicillin now can be added. No

specific organisms were recovered in these cases; had they been, vaccines may have been of some help. Five of the 6 patients were operated on. From a careful review of the 6 cases, it seems clear that well timed surgical intervention is probably of greatest benefit in this disorder. Once immediate supportive therapy has been instituted, an ileostomy is imperative to sidetrack the fecal stream. Moreover, in view of what Sweet has emphasized, i. e., that the colon in this condition can be excessively distended, cecostomy and/or appendicostomy together with pectinotomy of the anal sphincter are imperative to afford maximum decompression of and drainage from the affected colon.

SUMMARY

1. The clinical record and autopsy findings in a case of acute fulminating ulcerative colitis with peritonitis and extensive loss of bowel wall for its entire length are reported together with an analysis of similar records in the literature.

2. That this condition is probably different etiologically from the "fulminating" form of thromboulcerative colitis described by Bargen is emphasized.

3. The differential diagnosis in this condition is discussed.

4. Well timed surgical intervention in conjunction with general supportive therapy is stressed as the most valuable method of treatment.

PRIMARY PERITONITIS CAUSED BY FRIEDLÄNDER'S BACILLUS

Report of a Case with Recovery Following Sulfadiazine Therapy

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FROM 1882, when Friedländer [1] described a micro-organism which he believed was the causative agent of lobar pneumonia, to recent times, infections with Klebsiella pneumoniae were thought to be almost wholly concerned with pathologic changes of the lungs. This concept of Klebsiella infection underwent a change following the report of Baehr, Shwartzman and Greenspan [2] in 1937. In a study of 198 cases of Friedländer's infections, these workers were able to establish a definite diagnosis of primary infection of the respiratory tract in only 2 cases. In approximately 80 per cent of their patients the primary sites of infection were the gastrointestinal tract, the genitourinary tract and the biliary passages and liver. So impressed were these investigators by the paucity of primary respiratory infections caused by this organism that they proposed a change of the name from Klebsiella pneumoniae to Klebsiella friedländeri. Since 1937 there have been a number of cases of extrapulmonary Klebsiella infections reported. However, in reviewing the literature, we are unable to find any previous report of primary peritonitis caused by Klebsiella pneumoniae. Because of the unusual clinical course of our patient, we believe that the case bears reporting.

REPORT OF CASE

The patient, K. P., a 47 year old white man, a mechanic, was admitted to the Salt Lake County General Hospital on Nov. 6, 1945 at 6 p. m., with chief complaints of severe pain in the lower abdominal region, of five hours' duration, and nausea and vomiting for one day. Three weeks prior to admission he was affected with generalized abdominal discomfort, described as an ache with girdle distribution. The ache was constant, but the patient could obtain some relief by

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Miss Eleanor Willie conducted the bacteriologic studies.

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1. Friedländer, C.: Ueber die Schizomyceten bei der acuten fibrosen Pneumonie, Virchows Arch. f. path. Anat. **87**:319-324, 1882; Die Mikrokokken der Pneumonie, Fortschr. d. Med. **1**:715-733, 1883; Weitere Bemerkungen über Pneumonia —Micrococcen, ibid. **2**:333-336, 1884.

2. Baehr, G.; Shwartzman, G., and Greenspan, E. C.: Bacillus Friedländer Infections, Ann. Int. Med. **10**:1788-1801 (June) 1937.

lying very still. Although he said that there had been no febrility accompanied with chills, the patient stated the belief that for two or three nights immediately prior to admission he had had some fever. Morning vomiting, present occasionally for the past few years, was attributed to an "excess of phlegm." During the past year the patient had noted occasional night sweats. Because of the general abdominal discomfort, the patient had taken a liberal dose of a proprietary laxative, which had caused several loose bowel movements but had had no effect on his abdominal discomfort.

At 1 p. m. on November 6 the patient was sitting in his automobile when he was suddenly seized with sharp pain in the abdomen, which seemed to radiate from the right to the left lower quadrant and then to a lesser degree throughout the entire abdomen. The pain was of such intensity as to be almost intolerable. Nausea and vomiting accompanied the pain. Some measure of relief could be obtained by lying on his back with his legs drawn up, but this relief was not in any sense complete.

The past history revealed that the patient was treated at this hospital in 1937 for pneumococcic pneumonia, followed by empyema on the right side. The empyema was treated by rib resection and open drainage and resolved slowly over a period of three years. Since 1940 the sinus has been completely healed and symptomless except for occasional mild pain over the scar. A review of the systems revealed nothing of note except minimal dysuria with a little frequency and urgency of one month's duration. The family history was noncontributory.

Physical examination revealed a well developed, moderately obese white man in acute distress. The pulse rate was 92, blood pressure 130 systolic and 80 diastolic and oral temperature 101.6 F. There was minimal mucopurulent nasal discharge and slight pharyngeal injection. Examination of the chest showed dulness to percussion, diminished voice and breath sounds and tactile fremitus over the base of the right lung posteriorly. Breath sounds were vesicular in character. Both sides of the diaphragm descended well on inspiration. Many coarse, moist rales were heard posteriorly throughout both lung fields, which cleared when the patient was mobilized. There was an old, well healed scar in the right infrascapular region, where the sinus tract had previously been. Moderate involuntary spasticity was present over the entire abdomen. Palpation revealed generalized abdominal tenderness, which was exquisite in the lower part of the abdomen, especially in the right lower quadrant. There was rebound tenderness referred to the right lower quadrant. No definite borborygmi were heard. It was impossible to feel the liver, kidneys, spleen or any mass. Old bilateral inguinal herniorraphy scars were noted. Generalized tenderness, more pronounced on the right side, was elicited on rectal examination. The prostate was essentially of normal size, shape and consistency and was not tender. Prior to operation the white blood cell count was 18,000, with a pronounced increase in the neutrophils, and the hemoglobin was 12.5 Gm. There were numerous white cells in the urine. The impression prior to operation was appendicitis, probably ruptured appendix, with abdominal abscess or spreading peritonitis.

Operative Note (Dr. P. B. Price).—A McBurney incision revealed diffuse inflammation of all the exposed peritoneal surfaces. A quantity of cloudy, odorless peritoneal fluid appeared, which was alkaline in reaction. The cecal wall and adjacent ileum were thick and edematous. A short, rudimentary appendix, lying retroperitoneally in a posterior position, was removed, although it appeared grossly to be uninvolved in the inflammatory process. Subsequent histologic examination confirmed that impression. The abdominal incision was then extended medially to permit a more satisfactory search for the source of the infection. Turgid, acutely

inflamed coils of small intestine were encountered, which were matted together with fibrin, pocketing off collections of thin yellowish pus. The mesentery in particular was thick with edema and acute inflammatory reaction. There was no evidence of diverticulitis, perforation or intestinal obstruction. Cautious palpation showed that the upper part of the abdomen was less seriously involved in the inflammatory process than the lower part. The operator's opinion at this time was that the patient had primary peritonitis. Since the condition of the patient did not appear to justify further exploration, the incision was closed without drainage.

The results of the various specimens cultured are shown in the table. Klebsiella organisms from both the peritoneal exudate and the cultures of material from the throat showed the characteristic quellung reaction when mixed with Klebsiella type A antiserum. Antibiotic tests in vitro using a synthetic medium showed Klebsiella organisms completely inhibited by sulfadiazine at a concentration of 3 mg. Penicillin had no inhibitory effect at concentrations of 0.13 units to 5 units

Bacteriologic Studies

Date	Specimen	Culture	White Blood Cell Count
11/6/45	Peritoneal exudate	Numerous Klebsiella pneumoniae Few B. hemolytic anaerobic streptococci	18,000
11/10	Blood Material from throat	Sterile Klebsiella pneumoniae	19,000
11/11	Urine Blood Feces	Sterile Sterile Negative for Klebsiella organisms and other pathogens	12,500
11/12	Incision drainage	Klebsiella organisms Few diphtheroids Few gram-positive rods Few staphylococci	12,500
11/14	Incision drainage	Few Klebsiella organisms	13,000
11/15	Material from throat Stool	Negative for Klebsiella organisms Negative for Klebsiella organisms	12,500
11/17	Material from throat	Negative for Klebsiella organisms	13,000
11/26	Urine	Enterococci	11,000
11/27	Material from throat	Negative for Klebsiella organisms	10,000

per 0.5 cc. Results of urinary examinations were essentially normal with the exception of the first specimen, which showed numerous white blood cells. The Mantoux test elicited a negative reaction, and examination of a three day specimen of sputum revealed no acid-fast bacilli.

Intraperitoneal injection into 2 mice, cultures of material from the throat into 1 and cultures of material from the peritoneum into 1, resulted in fulminating Klebsiella infections which killed the micec in seventeen and twenty hours. Intracardiac injection of a culture into a guinea pig resulted in death in twenty-four hours from Klebsiella septicemia, peritonitis and meningitis.

The course of the patient was remarkably smooth. His temperature rose to 99.8 F. each afternoon until one week postoperatively, at which time his incision was opened at either end to establish free drainage. Following this the wound healed rapidly and cleanly.

At this time the patient presented signs and symptoms of a mild coryza, which disappeared three days later. Subjectively, he offered no complaints subsequent to the first week in the hospital. Postoperative therapy consisted in simultaneous administration of sulfadiazine and penicillin until the nature of the

infection was determined; penicillin was then discontinued because in vitro studies showed the organism to be inhibited by sulfadiazine but not by penicillin. The patient continued to improve and was discharged as cured on the twenty-sixth hospital day.

COMMENT

Although the impression of primary peritonitis was gained during the operation, the diagnosis was not considered to be reasonably established until corroborative bacteriologic studies had been made and additional studies failed to reveal other sites of pathologic changes caused by Klebsiella organisms. The primary sites of Klebsiella infection to be considered would be the following: the gastrointestinal tract, the biliary passages and the liver, the genitourinary tract and the lungs and upper respiratory tract. A brief consideration of each of these possible sources shows that the probability of this clinical picture originating from any of these sites on the basis of antecedent infection is remote.

Gastrointestinal Tract.—The means by which a Klebsiella infection could conceivably originate from this site would be (*a*) a perforative lesion of the stomach, appendix or small or large bowel, (*b*) an intra-abdominal abscess, periappendicular or otherwise, and (*c*), questionably, inflammation of the gastrointestinal tract. These possibilities were ruled out in the following manner: (1) normal operative conditions; (2) two successive stool cultures negative for Klebsiella organisms or other pathogens; (3) absence of the usual intestinal flora and feculent odor in the peritoneal exudate; (4) normal postoperative roentgenologic and fluoroscopic examinations of the entire gastrointestinal tract, and (5) the remarkably smooth postoperative course, which strongly suggests that no large degree of pathologic change in the bowel was present.

Biliary Passages and Liver.—When this part of the anatomy is infected with Klebsiella organisms, certain signs and symptoms are almost invariably noted. Stasis in the biliary tract plays an important role in predisposing to infection at this site. Boettiger [3] in reporting 2 cases of hepatic abscesses due to Klebsiella organisms pointed to the extreme rarity of this condition (25 reported cases since 1900), the septic course and the fact that conditions reported as primary hepatic abscesses are more likely secondary to intestinal or biliary infection. Perforation of the gallbladder is another possible source of peritonitis. According to Baehr and co-workers [2] more than 80 per cent (38 of 46 cases) of patients with Klebsiella infection of the biliary passages have demonstrable cholelithiasis. We believe that this potential source of infection may be eliminated in our case by the following facts:

3. Boettiger, C.; Weinstein, M., and Werne, J.: Primary Suppuration of Liver Due to Friedländer's Bacillus, J. A. M. A. **114**:1050-1055 (March 23) 1940.

(1) no symptoms of biliary obstruction noted in the history; (2) absence of septicemic history and absence of signs of septicemia during hospitalization; (3) no signs of tenderness in the right upper quadrant or hepatic enlargement at any time before or following operation; (4) postoperatively a normal functioning gallbladder and the absence of any cholelithiasis or common duct obstruction as evidenced by the Graham-Cole test; (5) absence of bile in the peritoneal exudate, and (6) the remarkably benign postoperative course.

Genitourinary Tract.—Reports of prostatic [4] and perirenal [5] abscesses caused by Klebsiella organisms have appeared in recent years. It is important to note that Klebsiella infections of the urinary tract are often associated with other organisms, viz., Escherichia coli, Bacillus pyocyaneus, and Proteus vulgaris. As with biliary infections, so here, stasis is apt to be encountered, with resultant kidney infection. In our opinion Klebsiella infection of the genitourinary tract is inconsistent with the clinical findings in our case for the following reasons: (1) absence of Klebsiella organisms in the urine on repeated cultures (absence also of E. coli, B. pyocyaneus and P. vulgaris); (2) normal urinary conditions with the exception of initial, mild pyuria; (3) normal excretory urograms; (4) normal psoas shadows and kidney outlines on the roentgenograms; (5) no tenderness in the costovertebral angle elicited at any time, and (6) normal prostate on digital examination.

Lungs and Upper Respiratory Tract.—In addition to acute Friedländer's pneumonia, chronic Friedländer infections of the lungs, nose and sinuses, ears and pharynx have been described. Because of the history of previous pneumonia complicated by long-standing empyema and because of the positive culture of material from the throat obtained four days after admission to the hospital, our main interest centered here as a likely primary source of the infection.

In view of the patient's history, it would seem unnecessary to discuss any of the aforementioned conditions except chronic Friedländer infection of the pharynx and of the lungs. Chronic Friedländer infection of the lungs, as reported by Solomon,[6] is a proved, although probably not generally recognized, disease which could conceivably give rise to a picture of this type. The history of morning cough, "excess of phlegm" and occasional night sweats at once suggested that

4. Pfeiffer, D. B.: Klebsiella Pneumoniae Bacteremia Due to Prostatic Abscess: Case with Recovery, Ann. Surg. **106**:1115-1118 (Dec.) 1937.

5. Kindall, L.: Perirenal Abscess with Gas Formation and Metastatic Pulmonary Abscesses Due to Friedländer's Bacillus: Case Report, J. Urol. **46**:555-561 (Sept.) 1941.

6. Solomon, S.: Chronic Friedländer Infections of Lungs: Report of Seventeen Cases and Observations on Therapy with Sulfapyridine and Sulfanilamide, J. A. M. A. **115**:1527-1536 (Nov. 2) 1940.

Klebsiella organisms might be culpable as an etiologic factor. In the 17 cases studied by Solomon, almost constant symptoms and signs were pleurisy, hemoptysis, chills and fever at the onset and complications consisting mainly of pulmonary abscess, empyema, pleural effusion and, less frequently, pulmonary fibrosis. Our reasons for rejecting the previously mentioned sites, with the exception of the pharynx, are as follows: (1) absence of pleurisy, hemoptysis, chills and fever since the patient's recovery from pneumococcic pneumonia and empyema eight years ago; (2) absence of history and physical findings of the previously listed complications; (3) normal chest on roentgenologic examition except for pleural thickening at the base of the right lung and (4) absence of antibodies (agglutinins or capsule-swelling antibodies) in the patient's serum for four weeks after admission.

Although Klebsiella organisms were cultured from the pharynx four days after admission, the patient at no time had signs or symptoms of clinical pharyngitis. It should be noted that the organisms were discovered there unexpectedly on routine cultures to determine a possible source of infection. Routine cultures of material from the throat show that approximately 5 per cent of the population harbor Klebsiella organisms.[7] It is possible that the pharynx was the portal of entry of the organism in our patient and that spread was by way of the blood stream to the peritoneum.

SUMMARY

1. A case of a condition believed to be primary peritonitis caused by Bacillus friedländeri is presented.

2. Under sulfadiazine therapy the patient made a remarkably rapid and smooth recovery.

3. As far as we can determine, this is the first case of primary peritonitis of this sort to be reported.

7. Bloomfield, A. L.: The Mechanism of the Bacillus Carrier State with Special Reference to the Friedländer Bacillus, Am. Rev. Tuberc. **4**:847 (Jan.) 1921.

BLOOD LEVEL OF PHENOL IN UREMIA

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FISHBERG [1] has defined uremia as "A complex auto-intoxication, the variegated clinical picture being the summation of the effects of retention of various urinary constituents." He showed that virtually every known urinary constituent has at one time or another been indicted as an etiologic factor in the production of this syndrome. Of the various retained excretory products, certain ones seem to play a primary role while others are entirely of secondary importance. Some of the manifestations of the uremic syndrome are as yet unexplained, among them various types of cutaneous lesions, pericarditis and others. However, through extensive investigations in recent years, an approach to the more important manifestations has been gained.

Raab [2] has postulated that the presence of catechol and phenol compounds is a highly contributory if not the main cause of the electrocardiographic changes and the physical signs of cardiac failure in uremic patients.

The gastrointestinal symptoms have been attributed by Mason and his associates [3] to: (1) the retention of urea, which (*a*) forms ammonium salts by bacterial decomposition in the alimentary tract and (*b*) prevents the disposition of guanidine; (2) guanidine intoxication, which in itself produces gastroenteritis, and (3) dehydration and acid-base imbalance, which are thought to be of secondary importance and are occasionally absent.

Respiratory symptoms have also been ascribed to retention of guanidine [3] and to acidosis.

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1. Fishberg, A. M.: Hypertension and Nephritis, ed. 4, Philadelphia, Lea & Febiger, 1940.

2. Raab, W.: Cardiotoxic Substances in the Blood and Heart Muscle in Uremia, J. Lab. & Clin. Med. **29**:715-734 (July) 1944.

3. Mason, M. F.; Resnik, H.; Minot, A. S.; Rainey, J.; Pilcher, C., and Harrison, T. R.: Mechanism of Experimental Uremia, Arch. Int. Med. **60**: 312-336 (Aug.) 1937.

Of the greatest interest have been the nervous manifestations of uremia. Mason and his co-workers [3] have expressed the opinion that uremic patients are "subjected to two major antagonistic influences—stimulation and depression." A deficit in the calcium ion concentration in the cerebrospinal fluid produces symptoms of irritation (restlessness, muscular twitchings, convulsions and similar signs). A deficit in calcium ions results primarily from phosphate retention. On the other hand, elevated cerebrospinal phenol has a narcotic effect which is productive of somnolence, apathy, disorientation and coma. According to Fishberg,[1] Becher has shown that the latter symptoms do not appear until the phenol enters the cerebrospinal fluid. Also complicating this "balance" is the retention of guanidine,[3] which can produce either irritative or depressive symptoms, depending on the level, on whether or not a central deficit of calcium ions exists and on other factors.

Needless to say that from these studies the postulate of a unitary basis of uremia has long been discarded. As mentioned previously, several investigators have shown conclusively that "phenol" is elevated in uremia. However, Roen [4] has pointed out that their tests of phenol were nonspecific, measuring not only phenol but "also such substances carrying the phenol grouping and its various substitutions as phenol itself, p-cresol, diphenol, indican, skatol, indole, and other related compounds."

Roen,[4] in his investigation of 30 uremic patients at the Cleveland Clinics, employed a new method of determining the level of phenol in blood, which was devised by Bernhart. By this method the reaction is highly specific for the phenol structure and there is only a 3 per cent technical error. From his studies he has concluded the following:

> The phenol level in blood is increased in renal failure accompanied by uremia.
>
> The blood phenol is elevated in all cases of uremia regardless of the type of renal failure.
>
> The blood phenol is not elevated in simple blood nitrogen retention where there are no uremic symptoms.
>
> The height of the blood phenol, though generally related to the uremic symptoms, is not in direct proportion to the intensity of the uremic state

The methods employed in our studies have been identical with those of Roen, since we have endeavored to substantiate the evidence he presented. Table 1 is a series of normal values determined on the blood of normal persons. These values give us a basis for considering 2.0 mg. per hundred cubic centimeters as the upper limit of normal for the level of phenol in the blood. Our method of determining the level of

4. Roen, P. R.: The Chemical Basis of Uremia: Blood Phenol, J. Urol. **51**:110-116 (Jan.) 1944.

urea in the blood is that of Barker.[5] The normal value varies between 10 and 20 mg. per hundred cubic centimeters. Normal values of urea in the blood appear in table 2.

In addition to the lists of normal values in tables 1 and 2, we have studied a small series of patients in whom there were no uremic symptoms and in whom renal pathologic changes were not a factor. Their cases, then, also constitute a table of normal values.

TABLE 1.—*Normal Values for Phenol in Blood of Normal Persons*

Subject	Mg./100 cc.	Mg./100 cc. Added	Mg./100 cc. Recovery	Per Cent Recovery
C	0.50	1.50	1.50	100
Ki	1.30	1.60	1.70	106
E	1.80	0.75	0.70	93
R	0.70	2.50	2.50	100
D	1.15	....	....	...
G	1.00	....	....	...
K	0.60	....	....	...
O	1.10	....	....	...

TABLE 2.—*Normal Values for Urea in Blood of Normal Persons*

Subject	Mg./100 cc.	Mg./100 cc. Added	Mg./100 cc. Recovery	Per Cent Recovery
A	12.5	12.5	13.5	108
B	15.0	25.0	27.0	108
G	16.2	....	....	...
K	18.8	....	....	...
O	15.0	27.5	27.0	98
M	....	50.0	48.0	96
	....	75.0	73.0	97
C	12.0	25.0	25.5	102
Ki	18.0	50.0	51.0	102
E	13.0	....	....	...
R	16.0	....	....	...

TABLE 3.—*Values for Urea and Phenol in Cases of Patients Without Uremic Symptoms*

Case	Diagnosis	Urea	Uremic Symptoms	Phenol
1	Pernicious anemia	9.25	0	1.75
2	Normochromic anemia	22.50	0	1.80
3	Aleukemic myeloblastic leukemia	10.0	0	1.08
4	Hodgkin's disease	9.0	0	1.20
5	Hodgkin's disease	9.5	0	1.80
6	Chronic myelogenous leukemia	18.0	0	1.55
7	Lymphogenous leukemia	28.0	0	1.14

5. Barker, S. B.: The Direct Colorimetric Determination of Urea in Blood and Urine, J. Biol. Chem. **152**:453-463 (Feb.) 1944.

After the manner of Roen we have divided our patients into several categories according to the types of renal dysfunction. Since our interest has been primarily concerned with urologic problems, the majority of our patients are those suffering from various types of obstructive uropathy. Table 4 shows a series of 20 cases of postrenal obstructive uropathy.

TABLE 4.—*Values for Urea and Phenol in Cases of Postrenal Obstructive Uropathy*

Case	Date	Diagnosis	Urea	Uremic Symptoms	Phenol
8	6/19/44	Benign prostatic hypertrophy; overflow incontinence	62	++	2.18
9	7/24/44	Carcinoma of the urethra; complete retention	58	++++	3.20
10	1/20/45	Carcinoma of the bladder, with ureteral obstruction	158	++++	5.10
11	6/14/44	Carcinoma of the prostate	134	+++	2.85
12	6/13/44	Metastatic carcinoma of the rectum; ureteral obstruction	64	++++	2.25
13	6/15/44	Benign prostatic hypertrophy; complete retention	154	+++	10.80
14	2/13/44	Carcinoma of the prostate; complete retention	33	+++	2.40
15	6/22/44	Benign prostatic hypertrophy	54	+++	2.04
16	6/23/44	Carcinoma of the prostate; extension to ureters	132	++	2.98
17	8/ 4/44	Benign prostatic hypertrophy; complete retention	95	++++	7.20
18	7/ 3/44	Carcinoma of the prostate	75	0	2.40
19	1/30/45	Benign prostatic hypertrophy; 10 days after cystostomy	75.5	+	1.40
20	6/15/44	Benign prostatic hypertrophy; complete retention; 2 days after transurethral resection	28	0	4.0
21	6/19/44	Benign prostatic hypertrophy; 7 months after cystostomy and 9 days after transurethral resection	64	0	2.40
22	7/ 5/44	Vesical neck contracture after sodium chloride administered orally and sodium bicarbonate	60	0	2.20
23	6/14/44	2 yr. after cystectomy and bilateral cutaneous ureterostomy	146	0	5.42
24	8/15/44	Benign prostatic hypertrophy, with overflow incontinence	19	0	2.46
25	1/30/45	Benign prostatic hypertrophy; obstructive uropathy; postcatheter drainage and fluids administered intravenously	60	0	1.41
26	7/ 5/44	Benign prostatic hypertrophy	18	0	1.70
27	8/11/44	Benign prostatic hypertrophy; vesical calculus	29	0	1.65

From the values given in table 4, several broad generalities may be made:

1. In the majority but not all of the cases of postrenal obstructive uropathy with nitrogen retention, the level of phenol in the blood is elevated.

2. Uremic symptoms, while frequently present, are not always related to an elevated level of phenol. This applies not only to uremic symptoms in general but especially to symptoms of narcosis.

3. No parallelism occurs between the intensity of the uremic symptoms and the blood level of phenol.

4. There is no proportionate correlation between the blood levels of urea and phenol.

While our series of primary renal disease is small (table 5), the preceding conclusions apply in this type of pathologic changes too.

Only 1 case of prerenal azotemia was studied. The patient was a 49 year old man with traumatic rupture of the right kidney. Urinary output was exceeding 2,000 cc. per twenty-four hours at the time the determinations of blood chemistry were made. The value for urea was

TABLE 5.—*Values for Urea and Phenol in Patients with Primary Renal Disease*

Case	Date	Diagnosis	Urea	Uremic Symptoms	Phenol
28	1/11/45	Chronic nephritis, hypertension	46	0	2.15
29	8/11/44	Malignant hypertension	73	++++	1.62
30	1/10/45	? Acute hemorrhagic nephritis	38	++	1.90
31	6/26/44	Chronic active glomerulonephritis	88	+	3.12
32	7/21/44	Chronic active glomerulonephritis	132	+	1.85

TABLE 6.—*Level of Phenol in Blood of Patients Who Died*

Case	Date	Days Before Death	Phenol
10	1/20/45	9	5.10
	1/20/45	0	5.12
12	6/13/44	4	2.25
16	6/23/44	112	2.98
29	8/10/44	10	1.62
31	6/26/44	45	3.12
32	7/21/44	48	1.85
	8/10/44	28	1.63
	8/23/44	15	2.87

TABLE 7.—*Reversibility of Level of Blood Phenol*

Case	Date	Diagnosis and Therapy	Urea	Uremic Symptoms	Phenol
9	7/24/44	Carcinoma of the urethra; complete retention	58	++++	3.20
	7/27/44	1 day postoperatively after cystostomy	37.5	0	1.85
11	6/14/44	Carcinoma of the prostate; obstructive uropathy	134	++++	2.85
	6/19/44	Drainage by catheter; forced fluids	76	+++	2.40
	6/28/44	Drainage by catheter; forced fluids	38	0	2.85
	7/ 3/44	3 days postoperatively after transurethral resection	52	0	1.51
	7/18/44	18 days postoperatively after transurethral resection	32	0	1.62
13	6/15/44	Benign prostatic hypertrophy; complete retention	154	+++	10.80
	6/16/44	Cystostomy; fluids administered intravenously	124	+++	4.85
	6/19/44	Fluids administered intravenously	38	?	2.85
	6/22/44	Fluids adminstered intravenously	24	?	3.80
	7/ 8/44		15	0	1.60
17	8/ 4/44	Benign prostatic hypertrophy; complete retention	95	++++	7.20
	8/ 9/44	Postoral lactate; forced fluids; drainage by catheter	18.5	0	1.90
	8/12/44	2 days postoperatively after transurethral resection	29	0	1.80
	8/18/44		46	0	1.63

42 mg. per hundred cubic centimeters, and that for phenol was 1.85 mg. per hundred cubic centimeters, there being pronounced (4 plus) uremic symptoms present.

The question also arises as to whether or not the level of blood phenol is of prognostic value. Table 6 shows the patients who died.

and table 7 demonstrates the reversibility of the level of phenol in the blood.

The reversibility of the level of phenol in the blood even when high levels are present, as in cases 13 and 17, indicates that the test cannot be of significant prognostic import.

Since this report embodies relatively few cases, the results are not conclusive. While we have not been able to demonstrate constancy of elevated phenols in association with uremic symptoms, we do know that there is a definite relation of increased phenol to nitrogen retention. In the light of experimental studies of other investigators, one questions whether phenol alone is responsible for the narcotic symptoms of uremia. Since guanidine has been indicted as a factor, simultaneous studies of this substance and phenol would be of value. Also, other investigators measured not only phenol but other related substances, and it is feasible that it is the total of phenol and its derivatives which actually produces the narcotic effect. Certainly, the exact role of phenol in the uremic state has not been completely ascertained, and the question is open for further investigation.

CORRECTION

In the article by Dr. George A. Johnstone and Dr. John E. Ostendorph entitled "Cholecystitis with Perforation," which appeared in the July issue (ARCH. SURG. **53**:1, 1946), the following footnote was omitted:

> The unabridged version of this article was accepted to meet the thesis requirements for the degree of M.Sc. (Med.) for graduate work in surgery at the Graduate School of Medicine, University of Pennsylvania [by Dr. Ostendorph].